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THIRD DECADE OF SPACE BIOLOGY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 24 Jul 81) pp 4-10

[Article by O. G. Gazenko and G. P. Parfenov]

[English abstract from source] The paper reviews the major results of experiments on microorganisms, plants and animals flown onboard space vehicles during the past two decades. To explain the experimental findings, it is hypothesized that living beings develop an indirect adaptation to gravity effects which has a bearing only on the phylogenetic process.

[Text] The results of research on space biology during the 1st two decades constituted a positive foundation for manned flights, while some have gained general recognition and are a useful contribution to various branches of biology.

But time marches on, and new problems are emerging in space biology. Some arise because of the further exploration of space (primarily due to longer duration of flights), others ensue from the general advances of biological science, while others yet are based on the results of current programs, since it is necessary in a number of instances to conduct more precise and specialized or, on the contrary, broader experiments.

We submit below the main advances in the area of general gravity biology, which were made as a result of experiments aboard space vehicles, and we have formulated new problems or those that have not been definitively resolved.

Unicellular Organisms and Tissue Cell Cultures

Several teams of researchers studied the survival, mutability and many other aspects of vital functions of unicellular organisms aboard biosatellites and other space vehicles. The results turned out to be unambiguous, and the conclusions of the researchers were essentially the same: weightlessness does not affect survival of unicellular organisms, does not affect any aspect of their vital functions and does not induce mutations [1-13].

The results of these studies conform with theoretical data on the range of cell dimensions and shapes. In unicellular organisms, molecular diffusion is the principal physical process that provides for life. It is generally recognized that a distance of about 1 mm is the maximum for effective diffusion in a living cell. Indeed, the dimensions and shapes of cells are usually such that no point within them is more than 1 mm away from the surface membranes. In the well-known hypothesis of E. Pollard [14] concerning the effect of weightlessness on cells, it is stated that this is possible only in systems where the polar effect of gravity is more effective than equally probably diffusion in all directions. This possibility is incompatible with reality. The top range of cell size is determined by physical laws of diffusion. A unicellular organism could reach a considerable size in one direction, sometimes in two, but it never increases in three dimensions.

There is a mathematical basis to the second size-limiting factor. It requires that the ratio of cell volume to its surface be constant, and that it not exceed appreciably 1:3. With increase in this ratio, the diffusion surface cannot meet the biochemical requirements of cytoplasm. We can see that the most elementary geometric figure that meets this requirement is a sphere with a radius of about 1 mm. The ratio will be retained if the increase in cell volume is associated with complication of its shape. However, complicated shapes of unicellular, free-living organisms make the cell division process difficult and reduce physical strength.

Results that led to analogous conclusions were obtained from experiments with cell cultures of animal tissues [15, 16].

There were particularly convincing experiments on cell tissue of human embryo lungs. The behavior of the cell culture in weightlessness was recorded by means of time-lapse photography using two movie cameras. A study was made of growth rate of the culture, changes in DNA content, movement of cytoplasm, karyotype, chromosome structure and other parameters. No differences were observed between the results of experimental and control experiments. Two types of electron microphotographs were taken to examine subcellular structures: in depth and scanning.

While we now have an explanation of the behavior of individual cells in weightlessness, such aspects as populations of unicellular organisms, dynamics of their growth and distribution in a medium require serious study. Many unicellular organisms have either negative or positive gravitaxis, because of which they create species-specific distribution patterns in liquid media, and they are maintained by active gravity-dependent bioconvection [17]. The usual distribution patterns that have adaptive significance are impaired in weightlessness and acquire different features.

The usual distribution of unicellular organisms may change in weightlessness, even if they have no gravireception. All microorganisms have fine selective chemoreception. At the present time, we know of more than 20 specific chemoreceptors that provide for optimum distribution of a population in accordance with the chemical gradients of the environment. If convection movement disappears in weightlessness and chemical gradients start to equalize, there will apparently also be a change in cell concentration, as well as culture growth rate. In our opinion, expressly this explains the changes in growth rate and concentration of unicellular organisms observed in several studies conducted in weightlessness [18-20].

Microorganisms are very responsive to cultivation conditions. Expressly this is the basis of commercial production of economically important microorganisms. Weightlessness creates good conditions for this. It affects distribution of cells in the medium, gradients of concentration of nutrients and proportion of liquid and gas phase surfaces.

At first, experiments with chlorella suggested that weightlessness speeds up the growth of this microorganism. Subsequently, this effect was found to be attributable to the physically substantiated distinctions of distribution of liquid over the hydrophilic surface of the algal cultivator in weightlessness, as a result of which there was considerable increase in area of the interface between gas and liquid phases. This improved conditions for exchange of gases in the algal culture and provided for faster growth than in the control. Use of a physically adequate control with reproduction of the larger interface in weightlessness revealed that there was no appreciable difference between experimental and control algae with respect to growth rate [21].

As a rule, weightlessness creates better conditions for cultivation of microorganisms; for this reason there is often a difference between ground-based and in-flight experiments in favor of the latter. Such a phenomenon is observed only when the other cultivation conditions are retained: composition of medium, temperature and for aerobes aeration. But researchers concentrated primarily on the behavior of a single, free-living cell in weightlessness. In this respect, the experiments yielded unequivocal results: its properties, functions and morphology remained unchanged.

Plants

Some definite results were obtained in the last two decades from studies of plants in space flights. Onboard experiments, which were corroborated by tests in clinostats, revealed that all stages of plant development can proceed normally in weightlessness: seed sprouting, formation of primary organs [22, 23], flowering and maturation of seeds [24, 25], somatic embryogenesis [26, 27]. There should also be no difficulty in establishment of primordial generative elements in weightlessness, and this process is continuous from embryogenesis to blooming. The reports of cosmonauts from the Salyut-6 orbital station about blooming of arabidopsis in the Phyton instrument demonstrated convincingly that one can grow higher plants aboard, from seed to next generation seed, with proper care.

Nevertheless, the study of higher plants in weightlessness involves major and often unrecognized difficulties. The fact of the matter is that plants have more intimate relations with earth's biosphere than animals and man. Animals and man are heterotrophic organisms. They appeared much later than plants, after the latter had prepared earth's surface for millions of years to receive heterotrophs. An oxygen atmosphere, abundant sources of nutrition and even protection against radiation appeared. It can be said that plants induced appearance of animals by vacating the top link in the feed chain.

But things are different in manned spacecraft. There, plants are placed in an environment prepared by and for heterotrophs. This arrangement is not to plants' liking. Animals adjust their internal environment rather precisely to a wide range of environmental changes, since they have a general control center--a nervous system. Plants do not have a general center. Their development and vital functions occur because of what plant physiologists call a "free play of hormones," which interacts with the constant change in environmental conditions. This is how seed sprouting, growth, flowering, maturing and death of plants occur. Plants react to critical environmental changes with evolutionary adaptations that animals do not have: more diversified means of reproduction, long dormant period, usually broader ecological adaptation and considerably more flexible morphology. In general, animal evolution could be compared to the travel of an arrow, which creates the impression that this travel has some goal, and perhaps it does have one. But evolution of plants resembles the tide: its front is all-encompassing, and it is difficult to determine its general direction. In the plant kingdom the struggle for existence is passive. Plants cannot depart from a habitat that has adverse living conditions without perishing. Nor can they tell what expressly they do not like. Plants react to adverse conditions by death, anticipation, decline, discontinuation of fruit-bearing and long-term genetic changes. At present, plants are waiting for biologists to learn how to conduct experiments with them aboard space vehicles.

The intimate relations between plants and the biosphere, which is functionally their internal environment, require absolutely accurate regulation in experiments of such conditions as temperature, illumination, composition of atmosphere and mineral nutrients. For plants are photosynthesizing organisms and breathe with all their cells that have access to light and atmosphere. There are still no devices aboard spacecraft in which optimum conditions for plants have been provided. Definitive experiments with higher plants in weightlessness have yet to be performed. It is imperative to refine methods of growing plants in weightlessness. For this purpose, critical onboard experiments must be conducted with laboratory greenhouses. The main purpose of these experiments is to obtain positive results, i.e., provide the necesssary conditions for raising plants. Not only seeds, but vegetative plant organs--tubers, bulbs, cuttings--will be used as sowing material.

It is known that in weightlessness there is marked change in appearance of plants because of disturbances in orientation of under- and above-ground organs [23, 28, 29], changes in epinasty of roots [29] and leaves [30], probable disappearance of nutational movements [31]. Since plant appearance is of adaptational significance, this cannot fail to affect harvest and biomass yield. It is necessary to study the quantitative patterns that related plant changes to parameters of practical importance. Obviously, there are certain other important questions referable to experimentation with plants in weightlessness. We can expect changes in their biochemistry, since replacement of cellulose with hemicellulose is predicted, as well as anatomical disturbances due to absence of load on support tissues and change in mode of vascular system function. Finally, one must test methods of normalizing root and leaf orientation in the absence of gravitropic stimulation and, in particular, check whether gravistimuli can be replaced by photostimuli for plant organs to grow in the required direction.

Insects

Previous studies have shown that weightlessness does not have an appreciable effect on the nature and duration of development, morphology, anatomy, biochemistry, survival, viability and behavior of the drosophila [32-34], flour beetle [33, 35] and ichneumon wasp [36]. Moreover, in an experiment aboard Cosmos-1129 using the "Gravity Preferendum" instrument, it was established that the drosophila does not notice a decline of gravity to zero, judging by exposure time and number of specimens that developed in zones with different levels of gravity [37].

With gravity in excess of 1 G, prolonged development of invertebrates is an exponential function of gravity force [38] up to levels at which development stops and the organism perishes. In weightlessness, one can probably find the threshold that is characterized by species-specific mass of organisms. Organisms whose mass is below this threshold will apparently not notice weightlessness. Organisms with greater mass will respond to it with morphological and functional changes. According to estimates, the threshold mass should constitute about 4 g [39]. Experiments aboard biosatellites where artificial gravity is created will make it possible to check the validity of theoretical conclusions.

The most interesting problem of sensitivity of organisms in weightlessness as a function of body mass can be solved experimentally within the next few years. Some invertebrate species are ranked according to mass in a way that seems to be specially suited for such research.

Fish, Amphibians and Birds

For a long time it was believed that gravity is the cause of animal-vegetative polarization of fish, amphibian and bird ovicells. It was believed that its influence during the period between penetration of sperm into the ovicell and first cleavage was a mandatory condition of normal development [40, 41]. Laboratory experiments revealed that this point of view is too categorical. As it was learned, with compensation of gravity development may proceed normally, while animal-vegetative polarity is established upon maturation of ovicells long before sperm penetration [42, 43]. In weightlessness aboard spacecraft, no disturbances were demonstrated in fish and amphibian development [44, 45]. The same applies to development of birds and Japanese quail, according to the results of the experiment aboard the Cosmos-1129 biosatellite.

Although onboard experiments dealing with development cannot be deemed to be of deciding significance, since there have been comments about the conditions under which they were conducted, the aggregate results, with consideration of laboratory data, indicate that gravity is not a mandatory condition of normal development. Rather, it has corrective and back-up, i.e., auxiliary, significance to dorsalization of embryos [46, 47].

There is reason to believe that separation of an organism into dorsal and ventral regions is an ancient, and perhaps even the first morphological invention of the cell, its first phylogenetic reaction to existence in a world that has a top and bottom. In both animals and plants, the plane of the first embryonic division that determines which part is to be the back and which the abdomen, which are to be the apices and radices, cannot be altered by any means [48, 49]. Obviously, implementation of genetic instructions referable to this stage of development does not depend on exogenous conditions.

Nevertheless, it is necessary to conduct deciding critical experiments on development of living organisms in space vehicles. Moreover, since weightlessness is probably not an obstacle to normal development, the task emerges of checking through onboard experiments the efficiency and reliability of equipment used to raise and keep fish and birds for practical purposes.

Genetic Studies

The results of experiments using a large number of objects (from viruses to mice) demonstrated that weightlessness does not elicit an appreciable increase in incidence of either spontaneous or radiation-induced mutations. The hypothesis that mutations are induced only by factors of a quantum, fluctuating and discrete nature and, furthermore, must reach the gene to have a direct effect on it was confirmed [50]. However, there is one important exception to this thesis. In experiments with tradescantia and the drosophila, appearance of aneuploid somatic cells was repeatedly noted, which means that there were genomal mutations. Mutations of this type do not occur always, and their incidence depends on duration of flights [51-54]. However, the possibility of an increase in incidence of genetic changes is still an alarming signal, and makes it imperative to conduct a comprehensive study of the reality of this phenomenon and its quantitative patterns.

Nature of Biological Adaptation to Gravity

Numerous experiments performed for two decades aboard artificial earth satellites and other space vehicles furnished valuable material to space biology. The most important finding of practical value is probably proof that gravity does not affect intracellular processes so long as its magnitude does not make molecular diffusion of substances--metabolites--more difficult. The constancy of the rate of the mutation process in weightlessness, at least with regard to gene and chromosome mutations, is in essence a corollary of the first statement. From it ensues a second corollary, that the incidence of radiation mutations is unchanging. This means that exposure to ionizing radiation in space is not much more hazardous than on earth.

Figuratively speaking, the results of the studies revealed that man can rely on DNA during space exploration. The future will tell whether DNA can rely on man.

However, theoretically speaking, the state of affairs in space biology appears at first glance to be confused and even contradictory. It seems obvious that organisms depend on gravity, since this force is inseparably linked with the appearance of planets, existence of planets and living conditions on them. At any given point, gravity is directed toward its center. This imparts to everything, including living organisms, a universal arrangement that one can call approximately vertical. The solid, liquid and gaseous environments are separated by virtue of gravity in accordance with their densities. It participates in cyclic processes of convective movement of substance. In brief, gravity creates primary order, without which there would not be any physical conditions for life and biological evolution. In spite of these indisputable theses, as is evident from this survey, we find in experiments and observations very few biological processes that are influenced by gravity. Perhaps there are no such processes at all in organisms of relatively small size and mass. There are few exceptions, and all of them are related to the function of a multicellular organism as an integral whole. Of course, the arrangement of statocytes is also an exception; these are cells that are specialized for reception of gravity by means of statoliths, which are inclusions with high relative density. In plants, gravity possible participates in regulation of phytohormone transport. In large terrestrial vertebrates, the distribution of body fluids is determined by hydrostatic laws that depend on gravity conditions.

The situation appears paradoxical: on the one hand, we see that the entire morphology and vital functions of biological species (from prokaryotes to vertebrates) are obviously adapted to existence in a gravity field; on the other hand, we are unable to detect a single elementary biochemical or physiological process that would be stimulated, inhibited, triggered by gravity or related to it in some other way. In our opinion, this paradox is resolved by two theses:

1) Living organisms are not adapted to gravity at all; the fact of the matter is that they are adapted to environments formed by gravity which have a vectorial physical organization. Thus, there is indirect adaptation to gravity, which appears to be at least secondary, and more often of higher order.

2) There is phylogenetic meaning to the observed adaptation, i.e., this is a unitary continuous process, the duration of which equals the duration of biological evolution on earth. Its mechanism is the same as that of any evolutionary change--onset of random mutation events and selection of organisms in accordance with their adaptive values in the next generation.

The dorsoventral morphology of unicellular organisms and geotaxic behavior of prokaryotes are phylogenetic adaptations. By virtue of the process of progressive autonomization of the genotype in modern organisms, appearance of these structures and functions occurs independently of gravity. Upon establishment of polarity, the series of genetic changes on the molecular level, which are controlled by random events, is combined with natural selection into a determined morphological macrostructure. The interval between the start and end of this process constitutes hundreds of millions of years, while differences in complexity, according to some estimates, reach 10^{18} [55].

Within the framework of the expounded hypothesis on the nature of effect of gravity and adaptation to it, there is a good explanation for the morphological stability of organisms with change in gravity. We have already mentioned that efforts have consistently failed with regard to alteration of polarity by different means, including weightlessness and accelerations. It should be expected that during long-term space flights and aboard permanent orbital and planetary stations, where weightlessness or low gravity will be an important element of the habitat for many generations, not only the main physiological and biochemical processes, but basic morphology of living organisms will remain unchanged.

Two special problems merit special consideration: the possible change in usual geometric shapes of plants due to disappearance of geotropic reaction and formation of the skeletomuscular system of large terrestrial vertebrates, for whose normal development a prolonged postembryonic mechanical load is probably necessary.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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DIET OF CREW IN SALYUT-6 ORBITAL STATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 30 Jun 81) pp 10-13

[Article by V. P. Bychko, A. S. Ushakov, S. Kalandarov, M. V. Markaryan, Ye. A. Sedova, A. K. Sivuk and O. S. Khokhlova]

[English abstract from source] The space diets used in flight of five permanent Salyut-6 crews were instrumental in assuring their adequate nutritional status and work capacity required to fulfill flight programs. Some of them complained that sterile canned foods became distasteful; due to this, a space diet consisting of 65% freeze-dried foodstuffs was developed and tested.

[Text] The nutrition factor is given an important place in life support systems (LSS) for spacecraft crews. It consists of the food allowance and equipment to store foods, preparation and intake of food. The main purpose of this factor is to keep a level of vital functions in cosmonauts that would assure the successful implementation of flight programs. The distinctions of outfitting nutrition elements depend on both the duration of space missions and principles of construction of LSS as a whole.

Methods

In developing the food for crews in the Salyut-6 orbital station, due consideration was given to the experience of prior manned flights performed in the Soviet Union and United States, particularly aboard the manned Salyut series of orbital stations [1-3].

The nutritional provisions aboard Salyut-6 consisted of the following elements: food allowance, containers for stowing and storing foods, table to take meals, electric warmer, eating equipment (place settings), device to recycle water, measure and place hot and cold water into packs with dehydrated foods, containers for disposal of packages and leftover food.

The composition of the food allowance and results of testing it in model experiments and during three main missions were reported previously [2, 4]. The food allowance consisted of about 70 different foodstuffs and dishes. It was broken down into a 6-day menu and consisted of combinations of foods preserved by sterilization (about 80%) containing the usual amount of moisture and dehydrated foods (about 20%) reconstituted with hot or cold water prior to consumption. When they consumed the entire allowance, the crew members took in the following average amounts of assimilable foodstuffs per kg body weight: 1.5 g protein, 1.4 g fat, 4.5 g carbohydrates. The mean daily allowance contained 0.8 g calcium, 1.7 g phosphorus, 0.4 g magnesium, 3.0 g potassium, 4.5 g sodium and 50 mg iron. In addition to the vitamins contained in the food allowance, the crew members took an Undevit multiple vitamin lozenge twice a day and, starting with the second main mission, Aerovit [in the same dosage] which keeps better. The diet was well-balanced in all essential ingredients, as determined in a study of metabolism of subjects in ground-based model studies [2, 5-8].

After each main expedition, the diet was improved, primarily by widening the assortment of products and dishes and replacing foods that were rated poorly. The initial nutritional value of the diet was retained.

A proper meal schedule is very important to both assimilation of food and maintenance of a high work capacity of the cosmonauts. The crews had four meals, with close to uniform distribution of caloric value and amounts in all of the meals. The intervals between meals ranged from 3 to 5 h, depending on caloric value and amount. Determination was made of the optimum correlation between food intake and other forms of activity. On the basis of the concrete characteristics of sets of exercises used and onboard food allowances, it was deemed permissible to have 15-20-min intervals between exercise and intake of food, and intervals of 1-1.5 h between food intake and exercise. The most important and intensive work requiring high mental work capacity was scheduled no sooner than 1-1.5 h after intake of food [9].

During space flights aboard the Salyut-6 orbital station, intake of food was monitored. Metabolic parameters were examined mainly before and after the missions [2, 8].

During the flights referable to five main missions, in addition to the regular food allowance and in accordance with the wishes of crew members, a rather wide assortment of foods and dishes was delivered by the Progress cargo craft, Soyuz and Soyuz-T transport craft. These foods consisted of fresh vegetables and fruit, seasonings, fruit and berry juices, beverages, as well as a rather wide assortment of newly developed dehydrated and canned foods and dishes to be included in the diet of crews of future space vehicles. Thus, there was some excess of foodstuffs aboard Salyut-6 orbital station almost all of the time.

Results and Discussion

The results of flights referable to five main missions (95-, 140-, 175-, 185- and 75-day flights) revealed that the nutrition element functioned well as a whole, maintaining an adequate level of cosmonaut work capacity to implement the program.

The Table lists data on changes in weight of 10 crew members of the main missions in the course of the flights.

Dynamics of weight of crews of main missions aboard Salyut-6 station

Mission	Crew member	Body mass			Change in body mass	
		recom-mended	pre-flight	after landing	kg	%
First	CDR	67,3	74,4	71,2	—3.2	4,3
	FLE	75,5	82,0	77,6	—4.4	5,3
Second	CDR	71,3	84,5	82,4	—2,1	2,5
	FLE	76,4	75,0	68,6	—6.4	8,5
Third	CDR	65,9	81,7	76,2	—5.5	6,7
	FLE	82,3	84,0	84,2	+0.2	0,2
Fourth	CDR	69,1	70,2	70,8	+0.6	0,9
	FLE	82,3	86,5	90,0	+3.5	4,0
Fifth	CDR	71,3	83,0	81,2	—1.8	2,1
	FLE	74,1	73,2	70,1	—3,1	4,2

It should be noted that, according to the data from the onboard mass-meter, the crew of the fourth main mission gained weight during the flight. By the 182d day, the commander (CDR) gained 3.3 kg while the flight engineer (FLE) gained 4.7 kg. The Table lists weight after landing. The CDR weighted about 72 kg (2.0 kg more than preflight) between the 1st and 10th postflight days. and the FLE weighed 91 kg (4.5 kg more than preflight). The differences in weight changes of cosmonauts listed in the table are apparently attributable to the degree of resistance to flight factors, individual metabolic distinctions and thoroughness of performing the set of preventive measures, which included exercise, lower body negative pressure (LBNP), nutrition, etc. The crew of the fourth main mission was the first to gain weight appreciably during the 185-day flight, and this is apparently attributable to meticulous performance of preventive measures and broad use of such appetite stimulators as onions, garlic and various sharp seasonings, which together resulted in taking an amount of food that exceed energy expenditure. These findings confirm once more the thesis that it is imperative to strictly regulate nutrition in flight. It should be consistent with the body's requirements, both quantitatively (caloric value) and qualitatively (particularly with regard to amounts of essential food constituents).

There were no changes (according to the crews' reports) in gustatory sensations in the course of the flights. There were no dyspeptic disorders. Bowel movements were regular (once a day).

All of the cosmonauts involved in the main missions reported that they became tired of sterilized canned foods at different stages of the flights (most often after the 2d month). In our opinion, this was significantly remedied by the inclusion of up to 20% dehydrated foods and dishes in the regular allowance, as well as additional foods, including fresh vegetables and fruit, that were brought to the station.

A diet variant was developed, in view of becoming weary of sterilized canned food, which consisted mainly (65%) of dehydrated foods reconstituted before intake with hot or cold water. It should be noted that most of these foods had been tested aboard the Salyut-6 station as part of supplemental assortments, and they were well-rated by crew members.

This food allowance consisted of the following: 159 g protein, 131 g fat, 396 g carbohydrates, 0.9 g calcium, 2.5 g phosphorus, 0.5 g magnesium, 3.8 g potassium, 6.1 g sodium and caloric value of 3300 kcal (13807 kJ). Intake of an Aerovit multiple vitamin lozenge was scheduled twice a day (at breakfast and dinner).

List of foods and dishes on the menu for 1 day. Breakfast: pork with sweet pepper (dehydrated)--40 g; Russian cheese--100 g; honey cake--45 g; prunes (dehydrated)--50 g; coffee with sugar--24 g. Lunch: jellied beef tongue--100 g; Praline candies--50 g; cherry juice with pulp (dehydrated)--40 g. Dinner: ham--100 g; borshch with smoked foods--165 g; Tallin beef with mashed potatoes (dehydrated)--52.5 g; Moscow brand rye bread [steeped in boiling liquid as part of culinary process]--45 g; cookies with cheese--25 g; apple juice with pulp (dehydrated)--30 g. Supper: cottage cheese with nuts (dehydrated)--50 g; assorted meats--100 g; enriched wheat bread--30 g; plum and cherry dessert (dehydrated)--50 g; tea with sugar--23 g.

Studies were pursued to test adequacy of the diet to body requirements both under ordinary conditions (5 subjects, 20 days) and in a pressurized chamber with ammonia content in the atmosphere increased to 2 mg/m^3 (4 subjects, 36 days). We measured several parameters in these subjects, which characterize the state of protein, lipid, carbohydrate, vitamin and fluid metabolism, functional state of the adrenals, activity of several enzymes, immunological reactivity and intestinal microflora. We checked weight daily and determined assimilation of the main nutrients and nitrogen balance.

As a result of these studies, it was established that there were no appreciable changes in health status of most subjects. Only one subject (Mo-v) presented furunculosis in the pressure chamber, which was correlated with the results of allergological tests (nonspecific sensitization to streptococcus and staphylococcus). By the end of the study, he lost 5.5 kg, which was attributable to his high initial weight (93 kg) and marked deviation from the recommended weight (73.2 kg) for individuals of his age and height.

In subjects who initially weighed 70±5 kg, weight changes were in different directions (from +1.8 to -1.9 kg).

The appetite of all subjects remained good throughout the study period. They gave a good rating to the items in their diet (4 and 5 on a 5-point scale). The allowance was adequate in amount and elicited a feeling of satiety. No dyspeptic disorders were observed. Assimilation of the main food constituents was as follows: 87% for protein, 96.5% for fat and 97.5% for carbohydrates. Nitrogen balance was positive. The other parameters measured did not deviate from the base level either when the subjects remained under usual conditions.

But when they were exposed to the conditions in the pressure chamber and elevated (to 2.0 mg/m^3) ammonis content in inhaled air, the following changes were demonstrated: decrease of α-cholesterol and α-lipoprotein in blood serum; decreased excretion in urine of thiamin and N_1-methylnicotinamide; increase in blood plasma and urine ascorbic acid level; decline of acetylcholinesterase activity of erythrocytes and nonspecific cholinesterase activity of blood plasma; decrease in concentration of blood sugar; increase in lipase and lactate dehydrogenase activity, with concurrent decrease in erythrocyte ATP; activation of adrenal function; decline of blood histamine and serotonin levels; change in immunological reactivity (decline), quantitative and qualitative composition of intestinal microflora.

It should be noted that the changes in the above-mentioned parameters did not exceed the range of physiological fluctuations, and most of them reverted to the background levels in the recovery period. Evidently, these changes should be interpreted as an adaptive reaction of the subjects to conditions in the pressure chamber with elevated atmospheric ammonia content.

Thus, the proposed diet maintains a normal health status and satisfactory nutritional status in the subjects, and it can be recommended for crews of future space vehicles under real flight conditions.

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EFFECT OF 48-DAY FLIGHT ON BLOOD AMINO ACID CONTENT IN THE CREW OF SALYUT-5

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[Article by I. G. Popov and A. A. Latskevich]

[English abstract from source] The study of the content of 17 amino acids in plasma of the Salyut-5 crewmembers (the first expedition) pre- and postflight demonstrated their time-course changes. This concerns mostly cystine and methionine. It is therefore recommended to improve the cystine and methionine content of space diets and to modify technological procedure of food preservation.

[Text] The concentration of free amino acids in blood plasma and extracellular fluid is closely related to dynamic equilibrium of processes of protein synthesis and breakdown in animals and man. The amino acids contained in extracellular fluid continuously change places with amino acids in cells of the organism. For this reason, the relative accessibility of blood plasma for laboratory tests and dynamic observation has long since drawn the attention of scientists concerned with questions of amino acid, nitrogen, protein and other forms of metabolism in animals and man.

However, technical and methodological difficulties in setting up such studies complicate substantially the matter of obtaining extensive and, particularly, repeated material for comprehensive investigation of metabolism of the entire amino acid spectrum. Until recently, there was also the problem of lack of highly productive, reliable analytical equipment simple to operate [1-3]. This is apparently one of the reasons why there are virtually no reports in the literature concerning amino acid metabolism in cosmonauts during flights varying in duration.

As for more or less precise data about the dynamics of levels of essential and nonessential amino acids in blood plasma of cosmonauts in the course of an actual flight, there is none at all in the literature. Of course, this is related to methodological difficulties of obtaining venous blood samples under the complicated sanitary and hygienic conditions of flight, which must be done repeatedly and at different stages of space missions. There are also problems with regard to preserving blood samples and transporting them to earth for examination.

Heretofore, all studies in our country and abroad have been limited to assays of free amino acids in blood plasma before and after flights or simulation thereof on the ground [4, 5]. Unquestionably, this diminishes the informative value of obtained data, makes it difficult to study the dynamics of amino acid metabolism under the influence of the numerous space flight factors, which are often in different directions.

Unfortunately, there are still very few such data concerning the status of amino-acid metabolism in cosmonauts under the influence of the set of flight factors. Yet such data are of value to the study of amino acid metabolism and, consequently, all protein metabolism at the time of completion of missions. Data obtained in this manner could be compared to preflight parameters of the same cosmonauts, as well as to concentrations of free plasma amino acids in representatives of other occupations under ordinary living conditions.

The study of free amino acids of blood plasma also yields some important additional objective data that refine our conceptions of dynamics of nutritional status of cosmonauts during flights varying in duration and difficulty, adequacy of the flight diet, intensity of amino acid metabolism and assimilation of amino acids from food. This would also yield more specific data about the process of expenditure of different amino acids for different processes of biochemical synthesis of protein sturctures in the body under the influence of the unique living conditions of cosmonauts in flight. Such information is important to further refinement of the chemical formula, food allowances, assortment and form of foods used in flight, determination of optimum mealtime schedule at different stages of long-term space flights.

This report deals with the results of a study of the dynamics of free amino acid levels in blood plasma of crew members of the Salyut-5 orbital research station (first mission), on the basis of data obtained before and after completion of a 48-day space flight.

Methods

Free amino acids of blood plasma of the crew of the Salyut-5 station (first mission) were assayed in venous blood samples, which were taken on a fasting stomach before the flight, during the scheduled clinicophysiological examination, and then on the first day after completion of a 48-day flight. The blood samples were centrifuged (10 min, 2500 r/min). Blood plasma was sealed in glass vials, frozen and transported in this form to the laboratory.

A Hitachi automatic amino acid analyzer (KLA-3B model) was used to assay amino acids in plasma samples prepared by the standard method. The analyzer operated by the method of ion-exchange chromatography, which is presently considered to be the most accurate. The studies of A. S. Ushakov, T. F. Vysotskaya and other authors confirmed the advantages of this method over paper chromatography or microbiological methods [1-3, 6, 7].

We determined the concentration of 17 free amino acids in the cosmonauts' blood plasma: essential--lysine, threonine, valine, methionine, isoleucine, leucine and phenylalanine; nonessential--alanine, arginine, aspartic acid, histidine, glutamic acid, glycine, proline, serine, tyrosine and cystine. Total amino acids of blood plasma, total essential and nonessential amino acids, proportion of essential and nonessential amino acids were estimated. The obtained concentrations of amino acids were considered both dynamically and as compared to amino acid content found by other authors under different conditions and previously used methods.

Results and Discussion

Table 1 lists concentrations of free amino acids in blood plasma assayed in blood samples from the commander (CDR) and flight engineer (FLE), which were taken before and after flight in the Salyut-5 orbital station (first mission).

Table 1. Free amino acids (mg%) in blood plasma of crew of Salyut-5 orbital research station (first mission) before and after 48-day flight

Amino acids	CDR			FLE			Blood plasma free amino acids in adults [8]
	pre-flight	post-flight	in-flight change	pre-flight	post-flight	in-flight change	
	A. Essential amino acids						
Lysine	3,83	3,95	+0,12	3,52	3,79	+0,27	1,0—4,0
Threonine	2,13	3,68	+1,55	2,99	2,94	—0,05	1,0—3,0
Valine	2,80	1,66	—1,14	2,06	1,36	—0,70	1,5—3,0
Methionine	0,46	0,25	—0,21	0,33	0,52	+0,19	0,3—0,7
Leucine	1,94	1,98	+0,04	1,47	1,56	+0,09	1,0—3,0
Isoleucine	0,92	0,76	—0,16	0,70	0,72	+0,02	0,5—1,0
Phenylalanine	0,74	1,19	+0,45	0,69	0,93	+0,24	0,5—2,0
	B. Nonessential amino acids						
Cystine	0,73	0,24	—0,49	0,57	0,33	—0,24	1,0—3,0
Tyrosine	1,02	0,75	—0,27	0,73	0,60	—0,13	0,6—2,0
Alanine	3,18	3,92	+0,74	2,44	3,02	+0,58	2,0—4,0
Arginine	1,16	1,93	+0,77	1,08	1,37	+0,29	1,0—3,0
Aspartic acid	0,11	0,49	+0,38	0,32	0,30	—0,02	2,0—5,0
Histidine	1,09	0,89	—0,20	1,29	1,26	—0,03	0,8—2,0
Glycine	1,37	1,79	+0,42	2,06	1,24	—0,82	1,0—4,0
Glutamic acid	2,90	2,85	—0,05	2,08	2,12	+0,04	0,7—4,0
Proline	2,40	1,29	—1,11	1,28	1,96	+0,68	0,5—3,0
Serine	1,41	2,02	+0,61	1,45	1,70	+0,25	1,0—2,0

There are difficulties, related primarily to quantitative assays, in physiological and hygienic analysis of concentrations of blood plasma amino acids obtained by any method. It is necessary to determine what we are dealing with in each concrete instance: the physiological norm and variations thereof, or deviations from it. Unfortunately, there is still no adequately validated, generally recognized, let alone officially approved, physiological norm for blood amino acid content.

Let us compare the data on levels of amino acids in cosmonauts' plasma obtained before the flight (see Table 1) to the figures cited by I. S. Balakhovskiy in the latest edition of BME [Great Medical Encyclopedia] [8]. It should be noted that this source does not give mean values, but tentative data on the basis of material from a number of authors which, of course, is more correct when the relevant physiological norms have not yet been worked out. We cannot fail to notice that this publication lists, in our opinion, too wide a range of concentrations of amino acids in plasma for healthy man. Perhaps, the results of assaying amino acids by different methods, in different age and occupation groups, with qualitative differences in diet, were listed in the same table. All this compels us to raise the question of a need to revise the concentrations of blood plasma amino acids, which had been considered to be virtually "standard" up to now, on the basis of using more sophisticated methods, with consideration of specific living conditions, occupation and diet.

The levels of most amino acids in cosmonauts' blood plasma before the flight were in the range of the tentative values given by I. S. Balakhovskiy in BME [8]. Lysine, valine, isoleucine, glutamic acid and proline content was close to the top of the range of concentrations he gave (see Table 1), threonine, methionine, leucine, alanine and serine were average in the CDR. The concentration of phenylalanine, tyrosine, arginine, histidine and glycine was closer to the bottom of the tentative ranges given. In the FLE, lysine and threonine content was close to the top range; the levels of isoleucine, glutamic acid and serine were average. The concentrations of valine, methionine, leucine, phenylalanine, tyrosine, alanine, arginine, glycine and proline were closer to the bottom range in BME [8]. In both cosmonauts, only the preflight concentration of cystine and aspartic acid was below the levels noted by other authors that were considered normal (see Table 1).

As for the concentration of aspartic acid given in BME [8], it should be noted that it appears to be obviously too high. In other textbooks, lower figures are given for "normal" aspartic acid content, for example, from 0.01 to 0.07 (average 0.03) mg% [9].

In both cosmonauts, cystine content was indeed below the values listed by other authors. Insufficient intake of cystine with food, for example, because of individual limitation of intake of leguminous foods, could have been one of the most probable causes of this phenomenon. As we know, when there is a shortage of cystine in the body it can be synthesized from methionine. In such a case, there should be some difficulties in supplying methionine and the level thereof in plasma should drop. Indeed, methionine content was low in both cosmonauts, and the methionine level was also lower in the FLE, who presented a lower cystine level in plasma. This reinforces even more the hypothesis of alimentary genesis of the observed low cystine and methionine content in the cosmonauts' plasma.

Immediately after termination of the flight, the levels of most amino acids in blood plasma continued to be in the range of the average tentative values listed in BME [8]. Cystine and aspartic acid levels in both cosmonauts were an exception, and so was valine in the FLE and methionine in the CDR. We have already discussed the distinctions of the "norm" for aspartic acid. As for cystine content, we should mention that it continued to decrease in both cosmonauts during the flight, and this was demonstrated against the background of a relatively low level thereof before the flight. We cannot fail to also call attention to the further decrease in methionine concentration in the course of the flight in the CDR, and metabolism of this amino acid is closely linked with cystine metabolism.

As for the dynamics of changes in blood plasma amino acid content, in the CDR there was a decrease in concentration of valine, methionine, isoleucine, cystine, tyrosine, histidine, glutamic acid and proline, with increase in the rest of the amino acids. In the FLE, there was a decrease in threonine, valine, cystine, tyrosine, aspartic acid, histidine, glycine and an increase in the rest of the amino acids. Thus, changes in the same direction--decrease--were noted in the two cosmonauts only with regard to valine, cystine, tyrosine and histidine; the same direction--increase--was noted for lysine, leucine, phenylalanine, alanine, arginine and serine. The changes in levels of the other amino acids were in different directions. In the absolute majority of cases, the demonstrated changes in concentration of amino acids were in the range of tentative values listed in BME [8].

During the flight, there was appreciable decrease in concentration of valine in both cosmonauts. Some authors consider this to be an adverse factor, since a decline of blood plasma valine is indicative of worsening or even impairment of protein metabolism and development of protein deficiency [3].

The decrease in plasma concentration of valine, as well as cystine and methionine (the latter only in the CDR) could be attributed, to some extent, to the prolonged intake of onboard food allowance and change in the protein part of the diet in flight, as compared to preflight diet.

Apparently, there were both common and individual reasons for the above-mentioned cases of decreased amino acid concentration in cosmonauts' blood plasma. Thus, because he found it distasteful, the CDR consistently ate little or none of the pasteurized cottage cheese furnished in tubes. Consequently, as compared to the FLE, he regularly failed to consume a number of amino acids, primarily essential ones. This could explain in part why expressly the CDR showed a decrease in many essential amino acids and to a greater extent than the FLE (particularly methionine, valine and isoleucine). The developing methionine deficiency could also have had an adverse effect on the body's cystine supply, as well as level thereof in blood. Indeed, blood cystine level dropped in both cosmonauts, but more significantly in the CDR. If we were to judge the amino acid group as a whole, the content thereof remained more stable in the FLE than the CDR.

The change in diet during the flight, as compared to nutrition on the ground, could have been a common cause of inflight changes in metabolism of several amino acids, particularly methionine and cystine. For example, grain products were represented in flight almost exclusively by bakery goods, the amount of which (about 150 g/day) was less than intake of such foods on earth. Moreover, the CDR had requested and consumed during the flight almost exclusively wheat bread baked of highly refined flour with low cystine content. Perhaps this was one of the reasons for the more marked decrease in this amino acid in his blood.

As we analyze the alimentary aspect of the obtained data, we cannot fail to note that, because of using canned meat and dairy products, both cosmonauts were constantly on a diet with an amino acid content that was limited expressly in methionine and cystine. This circumstance could also have an adverse effect on the dynamics of these amino acids and, perhaps, valine and others as well.

Table 2. Overall (summary) levels (mg%) of 17 amino acids in blood plasma of the crew of Salyut-5 orbital research station (first mission) before and after 48-day flight

Parameter of amino acid metabolism	CDR			FLE		
	pre-flight	post-flight	inflight change	pre-flight	post-flight	inflight change
Total amino acids	28,19	29,64	+1,45	25,06	25,72	+0,66
Essential amino acids	12,82	13,47	+0,65	11,76	11,82	+0,06
Unessential amino acids	15,37	17,06	+2,31	13,30	13,90	+0,60
Proportion of essential and unessential amino acids	0,83	0,79	—0,04	0,88	0,85	—0,03

Table 2 lists data referable to changes in total (summary) amino acid content in the cosmonauts' blood plasma. These overall indicators show that the body was totally provided with essential and nonessential amino acids, and that they were concentrated in the body's main transport system, which is blood plasma. In particular, the proportion of essential and nonessential amino acids enables us to assess the quantitative ballance of these essential and nonessential components of plasma, as well as nutrient properties of blood. Unfortunately, there are still no generally recognized physiological standards for these overall indicators.

In analyzing the data in Table 2, we were impressed by the increase in total amino acids, the sum of essential and nonessential ones, in both cosmonauts in the course of the flight. A more substantial rise of overall indicators was noted in the CDR. The impression is created that there was even some increase in total supply of amino acids in the course of the flight. However, there was a concurrent change in essential/nonessential amino acid ratio in the direction of a decline, and this causes us to be wary, since it indicates that the general increase in amino acid content of blood plasma occurred chiefly due to an increase in unessential, rather than essential amino acids. Such dynamics of amino acid metabolism can hardly be deemed to be good enough, since it could reflect development of some amino acid imbalance or partial deficiency of some essential amino acids. Perhaps, some nutritional amino acid imbalance caused them to be mobilized from intracellular structures. In analyzing the changes observed in amino acid metabolism, one should take into consideration, first of all, a number of nutritional factors: 1) when changing from the preflight diet, the inflight standard food allowance was reduced with regard to both nutrients and amino acids; 2) the assortment of foods was different, mainly a decrease in intake of dairy products, eggs and leguminous products; 3) instead of freshly prepared food, products were used in flight that had been submitted to severe heat processing, drying and prolonged storage after cooking at positive temperatures. All this could not fail to affect both the absolute amounts of amino acids in foods, and accessibility thereof to digestion and assimilation in the gastrointestinal tract. One should expect changes in function of various physiological systems of the organism with change in living conditions, prevailing environmental factors, distinctions of professional work and other factors, and this inevitably leads to a change in processes of synthesis of various substances, for which blood plasma amino acids are required. Consequently, there is also a change in endogenous amino acid requirement, and this should also be reflected in levels thereof in blood plasma.

Our findings lead us to several practical conclusions:

1. It is necessary for cosmonauts to adhere more faithfully to the established diet, particularly with regard to amino acid-rich foods when using isocaloric allowances of fixed composition during long-term space flights.

2. The onboard foods should conform as much as possible to the liking of cosmonauts so that they would be fully consumed during flights.

3. It is desirable to increase cystine and methionine content of onboard food allowance and preflight diet.

4. More progressive technological methods of preserving inflight food must be further refined in order to assure better preservation of amino acids in them.

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STATE OF DIGESTIVE SYSTEM FOLLOWING LONG-TERM SPACE FLIGHTS

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[Article by K. V. Smirnov, G. D. Syrykh, V. I. Legen'kov, L. G. Goland-Ruvinova, I. L. Medkova and L. I. Voronin]

[English abstract from source] In the crewmembers of four Salyut-6 long-term flights, enzyme excretory function of the gastro-intestinal tract was investigated. These studies included: gastric proenzyme, pepsinogen, and pancreatic enzymes, amylase and lipase, in blood and urine, trypsin in blood, intestinal enzymes, invertase and glycyl-L-leucine dipeptidase in feces, and lipids in feces. The results obtained demonstrated a correlation between changes in enzyme excretion and space flight duration and profile. After the 140- and 175-day flight the most marked changes in the digestive organs were seen; they manifested as a simultaneous increase in secretory function of the stomach and the pancreas. However, after the 185-day flight, in which advanced countermeasures were used, the above changes were less distinct.

[Text] At the present time, constant studies are pursued of the system of digestive organs of crews aboard Soyuz series spacecraft and Salyut orbital stations.

Comprehensive studies are pursued before and after space flights of different duration of secretion of digestive hydrolases and peristaltic-evacuatory processes in the gastrointestinal tract [1, 2].

These studies demonstrated consistent changes in digestive system function, the depth and severity of which are related to duration and conditions of space flights. It was established that weightlessness plays the leading role in the genesis of the demonstrated changes.

We submit here the findings from a study of secretory function of the gastro-intestinal tract following long-term space flights in the Salyut orbital station.

Methods

Assays were made of digestive enzymes--pepsinogen, amylase, lipase, trypsin and its inhibitory in blood, amylase and lipase in urine, invertase and glycyl-L-leucine dipeptidase in feces--in the crews of Salyut-6 orbital station before and after space flights lasting 96, 140, 175 and 185 days. Functional activity of the glandular system of the stomach, pancreas and small intestine is characterized rather well by the level of activity of digestive enzymes in blood, urine and feces.

The method of V. I. Tugolukov [3] was used to assay the gastric proenzyme, pepsinogen, in blood, that of G. F. Korot'ko [4] was used to assay it in urine; blood and urine amylase activity was determined by the method of Smith and Roe [5], trypsin activity and that of its inhibitor in blood were measured by the method of V. A. Shaternikov [6]. The method of I. L. Medkova et al. was used to examine blood and urine lipolytic activity [7]. In feces, we assayed intestinal enzymes--invertase, glycyl-L-leucine dipeptidase--using the methods developed in the laboratory of A. M. Ugolev [8]. Thin-layer chromatography was used to determine the lipid spectrum of feces (free cholesterol, cholesterol esters, nonesterified fatty acids--NEFA, phospholipids, mono-, di- and triglycerides).

Results and Discussion

There was considerable intensification of incretion of the gastrointestinal proenzyme, pepsinogen,* in the crew of the first mission aboard the Salyut-6 orbital station on the 1st day after their 96-day space flight: to 16.4 in the commander (CDR) and 14.6 in the flight engineer (FLE), and there was considerable (to 63.6) increase in elimination of this enzyme in urine of the CDR (Table 1). At this time, the FLE presented elevation of pancreatic lipase in blood, whereas this enzyme remained at a low level in the CDR. In both the CDR and FLE, there was a high amylase level in blood before the flight (360 and 670, respectively, versus the normal of 70-180). Immediately after the flight amylase activity diminished in both cosmonauts. Subsequent tests in the 30 days of the readaptation period revealed a stable level of this enzyme. By the 7th day of the readaptation period there was normalization of pepsinogen secretion, and incretion of pancreatic lipase also reached the background level; however, there was gradual activation of the pancreatic enzyme, trypsin, in blood of both cosmonauts. By the 30th day, blood trypsin activity increased to 8.6 in the CDR (1.4 in the background period) and 6.8 in the FLE (4.7 in background period). We observed an increase in blood trypsin activity in the CDR.

There were more appreciable changes in elimination of digestive enzymes after the 140-day flight (Table 2). On the first postflight day both cosmonauts presented an increase in incretion of pepsinogen, along with depressed elimination of this enzyme in urine, which was more marked in the CDR. Examination of incretion and excretion of pancreatic amylase revealed an increase in activity of this enzyme in blood of both the CDR and FLE. The FLE also presented increased elimination of this enzyme in urine. The first postflight day was characterized by significant increase in blood trypsin activity in the FLE, to 7.1 versus 1.9 in the background period, whereas no appreciable changes were demonstrable in elimination of this enzyme in the CDR. As a result of examining incretion and excretion of pancreatic lipase at this time, we demonstrated a tendency toward increased excretion of this enzyme. We failed to note any consistent changes in intestinal enzymes. However, there was further increase in incretion of plasmopepsinogen in the CDR and in amylase activity in blood of both cosmonauts on the 25th postflight day. Blood lipase activity was also drastically increased in both the CDR and FLE. At this time, incretion of trypsin and its inhibitor presented a tendency toward normalization. Subsequent studies of the functional state of digestive organs, pursued on the 43d day of the readaptation period, enabled us to establish the dynamics of the demonstrated functional changes in the glandular system of the stomach and pancreas. By this time, there was normalization of blood amylase activity in both cosmonauts, and we failed to demonstrate deviations either in uropepsinogen content, as compared to the base level. In spite of a tendency toward decline, blood lipase activity was still high: 126.0 in the CDR and 84.0 in the FLE.

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*All of the tested parameters are given in arbitrary units.

Table 1. Dynamics of activity of digestive enzymes in crew members following 96-day orbital flight

Parameter, conventional units	CDR				FLE			
	pre-flt.	postflight days			pre-flt.	postflight days		
		1	7	30		1	7	30
Blood serum:								
amylase	360,0	180,0	228,0	132,0	670,0	143,0	137,4	144,0
lipase	84,0	0,0	16,8	46,2	8,1	126,0	47,0	88,2
trypsin	1,4	2,3		8,6	4,7	4,8	6,2	6,8
trypsin inhibitor	334,7	388,0		616,7	340,0	380,0	593,0	380,0
Plasma:								
plasmopepsinogen	4,4	16,4		6,0	2,8	14,6	4,9	3,5
Urine:								
amylase	2,7	2,2	3,3		3,6	14,8	5,76	
lipase	6,2	7,8	8,8		1,1	7,0	0,0	
uropepsinogen	28,7	63,6	37,3		21,4	19,5	16,9	

Table 2. Dynamics of activity of digestive enzymes following 140-day orbital flight

Parameter, conventional units	CDR				FLE			
	pre-flt.	postflight days			pre-flt.	postflight days		
		1	25	43		1	25	43
Blood plasma:								
amylase	144,0	240,0	690,0	120,0	67,0	180,0	228,0	90,0
lipase	54,6	84,0	210,0	126,0	0,0	58,8	126,0	84,0
trypsin	5,2	5,7	6,2		1,9	7,1	4,8	
trypsin inhibitor	464,2	730,2	654,0		410,9	791,0	525,0	
Plasma:								
plasmopepsinogen	5,2	9,7	10,4		4,4	8,9	6,1	
Urine:								
amylase	6,6	6,0		22,4	6,2	27,0		21,6
lipase	0,0	9,1		42,0	3,1	3,4		1,7
uropepsinogen	36,6	7,6		27,8	50,6	20,5		24,1

Table 3. Dynamics of activity of digestive enzymes following 175-day space flight

Parameter, conventional units	CDR			FLE		
	pre-flight	post-flight days		pre-flight	post-flight days	
		1	8		1	8
Blood serum:						
amylase	270,0	396,0	222,0	90,0	336,0	360,0
lipase	46,2	111,3	142,8	71,4	147,0	
trypsin	3,8	0,9	12,9	6,7	4,8	
Plasma:						
plasmopepsinogen	4,9	11,8	4,8	3,7	14,6	
Urine:						
amylase	4,9	6,0	3,82	5,4	24,0	1,89
lipase	4,5	5,0	6,0	1,7	7,1	0
uropepsinogen	54,0	89,0	26,7	25,0	52,0	48,2

Table 4. Dynamics of activity of digestive enzymes following 185-day space flight

Parameter, conventional units	CDR			FLE		
	pre-flight	post-flight days		pre-flight	post-flight days	
		1	8		1	8
Blood serum:	•					
amylase	294,0	230,8	393,8	205,2	210,0	618,0
lipase	0	21,0	162,8	120,8	63,0	47,3
trypsin	2,4	2,4	7,1	14,2	5,7	5,7
trypsin inhibitor	654,0	555,4	603,7			
Plasma						
plasmopepsinogen	8,0	8,5	8,0	7,0	6,4	8,0
Urine						
amylase	1,4	36,6	7,4	7,3	28,5	10,2
lipase	4,4	0	0	1,1	0	0
uropepsinogen	40,8	21,6	25,0	24,5	7,7	9,0

An appreciable increase in pepsinogen incretion was demonstrated for 1 day after the 175-day flight: to 11.8 (preflight 4.9) in the CDR and 14.6 in the FLE (preflight 3.7) (Table 3). Concurrently, there was drastic increase in excretion of this enzyme in urine. At this time there was an increase in blood amylase activity in both the CDR and FLE, as well as some intensification of excretion of this enzyme in urine. There was also drastic activation of the lipolytic enzyme system. Activity of blood pancreatic lipase increased to 111.3 (preflight 46.2) in the CDR and 147.0 in the FLE (71.4 preflight). However, there was no change in excretion of this enzyme in urine.

Examination of intestinal enzymes in feces (invertase and glycyl-L-leucine dipeptidase) revealed differences in excretion thereof. Both cosmonauts presented a decrease in fecal invertase content: to 19.1 (77.4-99.0 preflight) in the CDR and 19.6 (84.2-102.3 preflight) in the FLE. Glycyl-L-leucine dipeptidase content increased to 50.0 (23.5 preflight) in the CDR and 49.7 (38.9 preflight) in the FLE.

On the 8th postflight day, blood pepsinogen content dropped to 4.8 in the CDR, with concurrent depression of excretion of this enzyme in urine. A somewhat elevated pepsinogen level in urine persisted in the FLE. At this stage, both cosmonauts presented an elevated level of blood amylase activity. The CDR also showed an increase in blood lipase and trypsin activity.

Examination of lipid spectrum of feces revealed an increase in NEFA content: to 32% (3% in the background period) in the CDR and 42.3% (6.2% in the background period) in the FLE. Triglycerides disappeared entirely from feces of both cosmonauts. These findings are indicative of intensification of lipid hydrolysis in the intestine, on the one hand, and change in absorption of free fatty acids, on the other.

On the first day after the 185-day space flight, no appreciable changes were observed in either cosmonaut with regard to excretion of digestive hydrolases (Table 4). On the 8th postflight day, the CDR presented an increase in blood lipase and trypsin activity and the FLE showed an increase in amylase to 618.0 (205.2 in the background period). The FLE also presented some increase in blood pepsinogen level. Examination of the lipid spectrum of feces revealed an increase to 25% in NEFA content (11% in the background period), 17.7% for monoglycerides and diglycerides (4.8% in the background period). This was associated with a decline to 4.1% in triglycerides (34.4% in the background period).

To sum up the findings, it should be noted that the first day after the 96-day space flight was characterized by an increase in activity of gastric pepsinogen and pancreatic lipase. Analogous changes had been demonstrated following 7-8-day flights, but they were more related to the body's stress reaction to the return to earth's gravity. However, as compared to the parameters referable to prior flights, which were normalized by the 25th day of the readaptation period, there was an entire chain of successive changes in enzyme secretion [or excretion] in the readaptation period following 96-, 140- and 175-day space flights (up to the 43d day after the 175-day flight). Activation of trypsin was demonstrated by the 31st day of the recovery period following the 96-day space flight, and activity of all three pancreatic enzymes increased at this stage after the 140-day flight. There was intensification of exocrine function of the pancreas immediately after the 175-day space flight and throughout the readaptation period (up to the 43d day). Such dynamics of digestive system function are indicative of a direct dependence of depth and severity of changes on duration of exposure to weightlessness. Inflight use of preventive measures and conditioning of cosmonauts are very important to development of changes in enzyme secretion in the gastrointestinal tract during the readaptation period. Thus, the marked changes in enzyme secretion noted after the 175-day flight were not present on the 1st day after the 185-day flight. These changes occurred only on the 8th day of the readaptation period. After this mission, the FLE, who had participated in the preceding 175-day space flight, presented less marked changes in these parameters than the CDR. These studies of enzyme secreting processes in the gastrointestinal tract following long-term space flights make it possible to work out recommendations for adequate nutrition of cosmonauts in the readaptation period.

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BIOLOGICAL VALUE AND SHELF LIFE OF CULTURED DAIRY PRODUCTS IN THE DIET OF COSMONAUTS

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[Article by I. A. Radayeva, G. A. Rossikhina, V. A. Usacheva, G. S. Poyarkova and S. P. Shul'kina]

[English abstract from source] Freeze-dried culture milk products--yoghurt with sugar, yoghurt with fruits and berries, acidophilic paste--were examined in the course of storage. The optimal time of their storage was determined, high biological value of protein and good viability of lactic acid microflora were demonstrated. These products are recommended to be incorporated into space diets.

[Text] Studies of Soviet and American researchers have shown that the extreme factors of space flights, as well as a diet of canned [preserved] food could lead to some changes in composition of intestinal microflora [1-4].

According to current physiological nutrition standards, milk and dairy products should constitute 30-35% of man's daily food allowance [5]. Optimum nutrition requires mandatory regular intake of cultured dairy products, which are readily assimilated and have not only nutritional value, but dietetic and therapeutic-preventive properties that improve digestion of food [6].

Cultured dairy products are readily assimilated by the body: they affect secretory activity of the stomach and intestine, as a result of which the glands of the digestive tract secrete more intensively the enzymes that accelerate digestion and enhance peristaltic (motor) capacity of the intestine. There is also more assimilation of cultured dairy foods due to partial peptonization of proteins in them, i.e., breakdown into simpler substances. Hydrolyzed milk protein is assimilated more readily by the body. There is 7-11 times more free amino acids in cultured dairy products than in fresh milk [7]. Vitamins synthesized by lactobacilli, which are very necessary to the human body, accumulate in cultured dairy foods.

These foods, which have a pleasant and tangy flavor, stimulate the appetite thereby improving the general condition of the body.

The dietary and therapeutic properties of cultured dairy products can be attributed to the fact that microorganisms and substances formed as the result of biochemical processes that occur when milk turns sour have a geneficial effect on the human body [8].

The great Russian scientist, I. I. Mechnikov, had already pointed to the dietary and therapeutic properties of cultured dairy products. In his opinion, the lactobacilli contained in such food are capable of settling in the human intestine and having a beneficial effect on the body. Mechnikov's theory was confirmed in new research. In particular, in was proven that Lactobacillus acidophilus and L. bulgaricus (the chief microflora of acidophilus paste and yogurt) are more resistant to alkali; there is a profusion of both in the intestinal contents 24-28 h after intake of such foods [9]. L. acidophilus and bulgaricus have equivalent bactericidal and antibiotic properties against certain deleterious and pathogenic bacteria: putrefactive, typhus and dysentery [9]. Thus, the dietary and therapeutic properties of cultured dairy products are based on bactericidity (capacity to depress development, decontaminate) of lactobacilli.

We submit here the results of our studies of biological value and shelf life of three cultured dairy products submitted to freeze-drying: sweet yogurt, fruit and berry yogurt and acidophilus paste.

These foods have a pure sour milk flavor, they are adequately sweet and are readily reconstituted in water at a temperature of 20-25°C (reconstituted in 15-20 min). The reconstituted foods consist of a homogeneous, semiliquid mass that is more solid in the case of acidophilus paste.

Methods

The freeze-dried cultured dairy products were packed in portions in packets made of polymer film. They were packed on a vacuum packing machine with nitration. The foods were stored at two temperatures: in a refrigerator at 4°C (control) and incubator at 25°C.

We tested both freshly prepared foods and products stored for 3, 6, 9, 10, 12 and 15 months. In the freshly prepared products, we examined physicochemical parameters, energy value, and determined biological value on the basis of assaying amino acid composition of the foods, comparing them to the so-called ideal amino acid scales. As the "ideal" scale, we used protein from hen's eggs, cow's milk and the amino acid scale recommended by the WHO Food and Agriculture Organization to estimate the amino acid score according to "percentage of adequacy." We determined the comparative characteristics of biological value of sweet yogurt, fruit-berry yogurt and acidophilus paste. During storage, we examined biochemical changes in butterfat: lipid fractions, free volatile fatty acids, total free fatty acids and fatty acid composition. Lipid fractions were demonstrated by thin-layer chromatography on a Gilford unit. Free volatile fatty acids were isolated by the method of vapor distillation. They were then separated on a liquid-gas Chrome-4 chromatograph. Fatty acid composition was determined by liquid-gas chromatography on the abovementioned chromatograph. Total free fatty acids were assayed by titrometry with preliminary extraction thereof in a system of solvents.

Results and Discussion

On the basis of testing the main chemical composition of freeze-dried cultured dairy products (fat, protein, carbohydrates, minerals), their energy value was found to constitute 2000 kJ (500 kcal) for sweetened yogurt, 1900 kJ (475 kcal) for fruit-berry yogurt and 1750 kJ (420 kcal) for acidophilus paste.

A comparison of biological value of cultured dairy products submitted to freeze-drying yielded the following results. Methionine is the limiting acid on the WHO FAO scale and scale of hen's egg amino acids. The amino acid score calculated from the scale of cow's milk amino acids indicates that isoleucine is the limiting acid in all of the products tested. The estimated amino acid score on the WHO FAO scale for virtually all of the other essential amino acids is in excess of 100, which indicates rather high assimilation of cultured dairy products. At the same time, these products were found to be overtly deficient in methionine and isoleucine.

The biological value of protein depends more on the leucine/isoleucine (L/I) ratio than on absolute levels thereof. According to D. Rose [10], the minimum requirement for adult males with regard to leucine and isoleucine, sufficient to maintain nitrogen balance, constitutes 1.1 and 0.6 g, respectively, with L/I of 1.8. This ratio constituted 2.3 for sweet yogurt, 2.4 for fruit-berry yogurt and 2.1 for acidophilus paste. Consequently, the freeze-dried cultured dairy products can be put in the following order according to biological value: acidophilus paste, sweetened yogurt, fruit and berry yogurt.

We observed gradual decline of organoleptic parameters of all products in the course of storage. The process of worsening of organoleptic properties was much faster in the case of incubator storage. In samples of sweetened and fruit-berry yogurt, there was appearance of heterogeneous curd consistency without appreciable change in flavor after 6 months.

After 10 months, the fruit-berry yogurt and acidophilus paste were removed from the storage incubator because of the mild sour fat taste. Sweetened yogurt was removed from the incubator after 12 months on the basis of organoleptic parameters. The change in organoleptic properties in the course of storage is related to changes in fraction composition of lipids.

The decline to 10% in amount of triglycerides during storage in fruit-berry yogurt and to 7% in sweetened yogurt was indicative of biochemical processes in butterfat. Such changes occur due to accumulation of steroids and carbohydrates related to oxidative processes in butterfat, and this is what was noted in the organoleptic evaluation.

Control samples stored in the refrigerator were given a score of 0.1-0.2 higher than samples stored at 25°C after 9 months of storage and 0.4-0.7 higher after 15 months. The organoleptic properties of foods stored in the refrigerator were rather high after 15 months and were rated as follows on a 5-point scale: 4.9 for sweetened yogurt, 4.6 for fruit-berry yogurt and 4.9 for acidophilus paste.

It was determined that reconstitution of all products increased during storage from 10 min to 15-20 min, titrated acidity in sweetened and fruit-berry yogurt increased by 9-12°T and in acidophilus paste by 10-15°T, which is apparently related to a change in total free fatty acids.

The foods were analyzed for demonstration of bacteria in the E. coli group, pathogenic staphylococcus and salmonella according to microbiological parameters. In both freshly prepared products and those being stored, none of the above bacteria was demonstrable.

Studies of survival of lactobacillus microflora of the foods revealed that it decreased by a factor of 10 in sweetened and fruit-berry yogurt after storage for 15 months at 4°C and by 10^2 for acidophilus paste, as compared to freshly prepared samples.

The data on survival of lactobacilli confirm the feasibility of long-termed storage of freeze-dried cultured dairy products at low plus temperatures; the quality of the products remains intact.

Analysis of the results of these studies warrant the conclusion that biochemical processes are the most active during the first 3 months of storage in the incubator. During this period, there were fluctuations of acidity, changes in fraction composition of lipids related to accumulation of steroids and carbohydrates, with corresponding decrease in triglycerides, monoglycerides and diglycerides.

During the first 6 months of storage, there is accumulation of volatile free fatty acids (formic, acetic, propionic, butyric), as well as volatile acids (caproic, caprylic, capric) with some decrease in amounts of several unsaturated fatty acids.

After storage for six months, processes of biochemical conversions in these products slow down under virtually all storage conditions.

The following conclusions can be derived from our studies. Freeze-dried cultured dairy products are readily assimilated and contain a lactobacillary microflora that can settle in the human intestine. These foods have a rather high biological value with respect to their protein: the leucine/isoleucine ratio constitutes 2.1 for acidophilus paste, 2.3 for sweetened yogurt and 2.4 for fruit and berry yogurt.

Testing the freeze-dried cultured dairy products in the course of storage enabled us to determine realistic shelf life thereof as a function of temperature: 12 months at 20±5°C and 18 months at 1-4°C.

Thus, freeze-dried cultured dairy products may be quite beneficial in the diet of cosmonauts.

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EFFECT OF HYPOKINESIA ON MAN'S NUTRITIONAL STATUS

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[Article by V. P. Bychkov, V. N. Gryaznova, S. Kalandarov, A. G. Kasatkina, V. A. Korshunova, M. V. Markaryan, A. K. Sivuk and O. S. Khokhlova]

[English abstract from source] In three series of experiments of 120, 49 and 180 days in duration 36 test subjects were exposed to clinostatic and antiorthostatic hypokinesia. Human requirements for various nutrients were defined under hypokinetic conditions. It was demonstrated that during bed rest exercises together with adequate nutrition and after bed rest certain nutrients can serve as efficient countermeasures against metabolic changes.

[Text] The purpose of these studies was to examine the effects of clinostatic and antiorthostatic [head end of bed tilted down] hypokinesia on some metabolic parameters in order to determine human requirements referable to the main nutrients under such conditions and to assess the efficacy of some preventive measures.

Methods

We conducted 3 series of studies lasting 49, 120 and 180 days on 36 healthy males.

In the first series [1, 2], 10 subjects 22-45 years of age were separated into 3 groups: the first consisted of 4 men, the second of 3 and the third of 3 men. The studies consisted of three stages: background--20 days, experimental--120 days and recovery--30 days. At the first and third stages the subjects were on the usual regimen at the hospital and in the second stage they maintained bed rest (in horizontal position, supine). The first group of subjects was submitted only to hypokinesia; the second group was given pituitrin up to the 40th day and deoxycorticosterone acetate (DOCA) from the 72d to 90th days to correct fluid-electrolyte metabolism. To correct protein metabolism, the third group was given the anabolic product, nerobol, according to a schedule [chart?]. The food allowance consisted of unadulterated products balanced in nutrient content. At the first and third stages, the diet contained about 100 g protein, about 86 g fat and about 416 g carbohydrates, and it had a caloric value of 2900 kcal (121,134 kJ); at the second stage, the figures were 86, 82 and 314 g, respectively, with caloric value of abut 2400 kcal (10,042 kJ). We collected and analyzed feces, urine and venous blood on "metabolic" days (11th-13th days of the first stage, 34th-36th, 69th-71st, 104th-106th days of the second, as well as 10th-12th days of the third stages). We assayed nitrogen, moisture, fat and ash in feces, relative density, pH, total nitrogen, urea, ammonia, uric acid, creatine, creatinine, free amino acids, epinephrine, norepinephrine, 17-hydroxycorticosteroids (HCS) and 17-ketosteroids (KS), vitamins, C, B_1, B_2 and 4-pyridoxic acid in urine. We analyzed blood serum for total protein and fractions thereof, free amino acids, total lipids, cholesterol, phospholipid phosphorus, lipoproteins, residual nitrogen, sialic acid, vitamin E and 11-hydroxycorticosteroids (11-HCS). In addition, we measured phagocytic activity of blood leukocytes and performed the glucose tolerance test after injection thereof intravenously. We also estimated extracellular fluid volume (EFV) [3].

In the second series of studies [4-6], 18 subjects 31-40 years of age were on bed rest for 182 days in antiorthostatic position, with the head of the bed tilted down at an angle of 4.5°. The subjects were divided into three groups (6 men in each) differing in degree of restriction of motor activity. During the period of hypokinesia, the first group of subjects performed a set of physical exercises with energy expenditure of about 400 kcal/day (1674 kJ) and the exercise of the second group constituted 200 kcal/day (837 kJ). No preventive measures were used in the third (control) group. At all stages the subjects were on a diet of fresh foods that was balanced in the main nutrients. The caloric value of the diet of all three groups constituted 3000 kcal at the first stage (12,552 kJ) with 110 g protein. During the experimental period, the caloric value of the diet was 3300 kcal (13,807 kJ) with 114 g protein for the first group, 2900 kcal (12,134 kJ) with 102 g protein for the second group and for the third group it constituted 2900 kcal with 102 g protein up to the 90th day, 2750 kcal (11,406 kJ) with 97 g protein after the 90th day. In the course of the studies we analyzed the following parameters in average daily urine specimens: total nitrogen, urea, creatine, creatinine, vitamins C, B_1 and 4-pyridoxic acid. We also analyzed total nitrogen in the food allowance.

In the third series of studies [7], we tested the effect of 49-day antiorthostatic hypokinesia (head of the bed tilted down at an angle of 4°) on the nutritional status of 8 subjects 36 to 40 years of age. To determine the nutritional status, we determined body weight, metabolism (protien, lipid, carbohydrate, vitamin and mineral) and digestive system function. This study consists of three stages: background (12 days), hypokinesia (49 days) and recovery (30 days). In the recovery period, the subjects in the main and control groups performed sets of physical exercises; on the first 3 days, energy expenditure constituted 836 kJ (200 kcal) and from the 4th day on 2090 kJ (500 kcal). The diet was strictly regulated and differentiated, in accordance with the stages of the study. The food allowance consisted of freshly prepared unadulterated products. It had a lower caloric value and contained lesser amounts of the main nutrients during the hypokinetic stage than in the background period. In the recovery period, the subjects were divided into two groups: the first group (control) (3 men) were on the same diet as in the background period, whereas the subjects in the second (main) group (5 men) received the recovery period diet (with food supplements). The nutritional rehabilitation measures involved additional amounts of sources of complete animal protein (42 g), polyunsaturated fatty acids (8 g), mineral salts (1.6 g potassium 300 mg calcium, 530 mg phosphorus, 60 mg magnesium) in the food allowance. The supplements were in the form of unadulterated foods (beef, cottage cheese, dried apricots). We assayed total protein and fractions thereof, free amino acids, cholesterol, total lipids, α- and β-lipoproteins, 11-HCS and vitamin E in blood serum and plasma of the subjects. We tested them for glucose tolerance. We measured the end products of nitrogen metabolism, catecholamine, HCS and ketocorticosteroid concentrations, vitamins C, B_1, B_2 and B_6 (4-pyridoxic acid) in 24-h urine. Balance studies of several elements (nitrogen, calcium, phosphorus, magnesium, potassium, sodium and chlorine) were conducted, and we estimated assimilation of the main nutrients.

Results and Discussion

Analysis of the data obtained from the first series of studies revealed that all of the subjects tolerated it well. Throughout the experiment, they presented some deviations in health status due to the side-effects of pituitrin and DOCA, which either disappeared spontaneously or after drug therapy. There was particularly difficulty in the transition from hypokinesia to the usual motor activity.

The subjects consumed their food allowance almost entirely. Assimilation of the main nutrients was as follows: ~88% protein, ~96% fat, ~98% carbohydrates at the first stage, ~90, 96 and 97%, respectively, at the third stage, i.e., it was not less during the hypokinetic period than in the background period. The subjects retained their initial body weight when given 1.1±0.07 g assimilable protein, 1.2±0.03 g fat, 4.4±0.28 g carbohydrates and 33±2.2 kcal/kg body weight, or 138±9.2 kJ ($M \pm mt_{95}$) energy, during 120-day hypokinesia, which is indicative of the adequacy of these amounts of nutrients to the body's needs.

These data can be used as base figures in preparing diets for individuals (test subjects and patients) under hypokinetic conditions. Under the influence of 120 days of hypokinesia we observed the following changes in the subjects: increased elimination of end products of nitrogen metabolism associated in most cases with a negative nitrogen balance; increased concentration of total lipids and cholesterol in blood serum, decrease in α-lipoproteins by the 35th day with subsequent return to background levels; diminished glucose tolerance in most subjects on the 26th, 66th and 96th days; changes in parameters characterizing the functional state of the adrenosympathetic system and adrenal cortex, which were individual in nature; diminished phagocytic activity of blood neutrophils with concurrent increase in sialic acid concentration of β- and γ-globulins; reduced EFV, which was particularly evident on the 6th and 66th days (by 2.7 and 2.2 ℓ, respectively). We failed to demonstrate appreciable changes in metabolism of vitamins C, B_1, B_2, B_6 and E.

We demonstrated the following changes after intake of nerobol by the subjects in the third group: decreased elimination of end products of nitrogen metabolism, which led to a markedly positive nitrogen balance (this effect was marked only on the 34th-36th day and not manifest on the 104th-106th days of hypokinesia); increased utilization of free amino acids from blood serum; considerable increase in blood serum concentration of total lipids, cholesterol and decrease in α-lipoprotein content (on the 70th day, when nerobol had not been given for over 1 month, these parameters presented a tendency toward normalization); decreased excretion in urine of vitamins B_1, B_2, 4-pyridoxic acid; decline of parameters characterizing functional activity of the adrenosympathetic system and adrenal cortex; increased EFV by 0.4-0.6 ℓ, respectively on the 6th and 26th days (when nerobol was given) and 0.9 ℓ decrease in EFV on the 66th day (1 month after discontinuing nerobol).

The EFV remained close to the initial volume in the second group of subjects who were given pituitrin and then DOCA.

The results of these studies indicated that there was no normalization of nitrogen metabolism in the subjects of the first two groups, so that special measures had to be developed [1, 2].

Most researchers believe that there is a decrease in synthesis of muscular nitrogen compounds during hypokinesia or some increase in rate of their breakdown, which leads to reduction of muscle volume and strength, and increased elimination of some end products of nitrogen metabolism.

Apparently, because of the decrease in protein synthesis there should be less expenditure of energetic material (carbohydrates, lipids) for this purpose, and under conditions of drastic reduction of expenditure of energy (hypokinesia) this leads to slower utilization of these products by cells and tissues and, consequently, to elevation of level thereof in blood and certain organs.

In our study, we found an increase in blood lipid components and decrease in glucose tolerance of most subjects on the 35th day of hypokinesia. Subsequent restoration of these parameters to the base level was apparently related to triggering of compensatory mechanisms of the body (increase in lipolytic enzyme activity and others).

The attempt to normalize protein metabolism by administering nerobol led to intensification of anabolic processes, but there was also mobilization of reserve fat for protein synthesis, which was associated with considerable increase in concentration of blood serum total lipids, cholesterol and decrease in α-lipoprotein content. Subjectively, these changes were associated with a poorer appetite. Apparently, these adverse changes in lipid metabolism must be taken into consideration, both in the practice of space flights and clinical medicine. Intake of nerobol was also associated with some androgenic effect (the subjects reported an increased sex drive with intake of this product).

G. P. Shul'tsev [8] and Arnold et al. [9] also believed that nerobol (methandrostenolone) has an appreciable andorgenic, as well as hepatotoxic effect, along with the anabolic one. No other studies have been conducted on the effect of this agent on lipid metabolism in healthy man. In view of our findings, it can be concluded that it is undesirable to use nerobol for normalization of nitrogen metabolism of hypokinetic humans.

The patterns of changes in the parameters studied under the influence of hypokinesia were analogous in the second and third series of studies to those demonstrated in the first series [4-7].

Analysis of the data obtained in the second series of studies, with regard to nitrogen and vitamin metabolism, revealed that there were insignificant deviations of the parameters studied from physiological standards. At the same time, the marked fluctuations thereof can apparently be attributed to the subjects' reaction to the beginning and end of the study, adaptation to hypokinesia and the set of preventive measures. The obtained data enable us to trace rather clearly the beneficial effect of the sets of preventive measures used on the tested parameters of nitrogen and vitamin metabolism. The most stable parameters of nitrogen metabolism, correlation between them, nitrogen balance and excretion of vitamins C, B_1 and 4-pyridoxic acid in urine were demonstrated in the second group of subjects, and this is apparently related to the conformity of energy expenditure on physical exercise to the level of their usual energy expenditure. These findings are indicative of the desirability of adaptation of the subjects in advance for the level of physical activity expected to be used for preventive purposes in weightlessness or its ground-based model--hypokinesia, so that this factor would not constitute an additional stimulus for the adaptive mechanisms of the body, that are already functioning intensively.

The findings from the third series of studies [7] revealed that there was prevalence of catabolic over anabolic processes under the influence of 49-day antiorthostatic hypokinesia. This was manifested by weight loss (by an average of 1.9 kg), as well as negative balance of nitrogen, phosphorus, potassium and sodium. The nutritional rehabilitation measures used on the 5 subjects of the main group led to a marked positive nitrogen balance (+3.0 g), increase in albumin fraction of blood serum protein, increased utilization of vitamins C, B_1 and B_6, and faster termination of compensatory nitrogen retention, as compared to subjects in the control group. These data are indicative of the efficacy of the nutritional factors used to restore man's functional state in the recovery period following long-term antiorthostatic hypokinesia.

Thus, our findings enabled us to determine human requirements referable to the main nutrients and to trace the metabolic distinctions during clinostatic (bed rest) and antiorthostatic hypokinesia. The changes were in the same direction, consisting of prevalence of catabolic processes over anabolic ones. Physical exercise against the background of adequate nutrition was found to be the most effective means of preventing changes observed under hypokinetic conditions, and this also applies to the food supplements added to the allowance in the recovery period following 49 days of antiorthostatic hypokinesia.

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CLINICOPHYSIOLOGICAL CHANGES IN MAN DURING LONG-TERM ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 22 Jun 81) pp 29-34

[Article by T. N. Krupina, A. Ya. Tizul, M. P. Kuz'min and N. I. Tsyganova]

[English abstract from source] By clinical-physiological and biochemical methods adpatation to prolonged (182 days) head-down tilting (-4.5") was investigated. It was found that man exposed to hypokinesia for a month or longer, with countermeasures lacking, showed polymorphic clinical-physiological and biochemical disorders accompanied by a decline of his adaptive capabilities. This may aggravate further adaptation and readaptation processes.

[Text] The increased duration of space flights puts several tasks to space medicine with regard to medical support, the performance of which can be fruitful only on the basis of deepening our knowledge of clinical and physiological phenomena occurring in man during space flights and clarifying the substance of pathogenetic mechanisms of development of the effects of weightlessness. The effects of weightlessness are simulated on earth by means of models with immersion medium or antiorthostatic [head-down tilt] hypokinesia (AOH).

In this work, we studied the clinicophysiological and biochemical changes in man resulting from prolonged (182 days) AOH in order to work out problems of predicting disorders and diseases of cosmonauts during space flights, as well as develop scientifically validated means of preventing and restoring impaired functions.

Methods

A total of 18 men 31-42 years of age participated in this study; they were divided into three equal groups of 6 men in each. For 182 days the subjects were on strict bed rest in antiorthostatic position (-4.5°). To gain more information about the mechanisms of development of clinical changes under these conditions, we included some subjects with deviations in health status: diminished adaptability of the myocardium to exercise in 2 subjects (first group); 4 men (second group) endured Master's double test satisfactorily and 2 men (third group) presented a tendency toward hypertensive reactions. The first group of subjects performed graded exercise with energy expenditure of about 700 kcal/day, the physical load was half this size for the second group of subjects, while the third group did not exercise at all and served as a control; this was done to determine the importance of exercise in preventing the adverse effects of AOH. We used traditional methods of clinical examination, measured diastolic pressure in the central retinal artery and intraocular pressure, and we determined some biochemical parameters (lipid, hormone metabolism and others).

Results and Discussion

The results of these studies and clinical observations, as well as data referable to long-term space flights, indicate that there is development of diverse functional disorders associated with diminished adaptability during space flights and in the recovery period in man submitted to antiorthostatic hypokinesia or weightlessness for 1 month or longer, in the absence or with inadequacy of preventive measures.

Studies of clinical and physiological changes during prolonged hypokinesia and during space flights revealed that, under the prolonged effect of AOH and space flight factors, one first observes functional (adaptive) disorders, and at later stages there is development of disturbances which, when they form a number of circumscribed clinical syndromes, could complicate subsequent adaptation and recovery processes.

The most frequently observed clinical syndromes referable to prolonged hypokinesia, which are also observed to some degree or other during space flights and particularly in the readaptation period, include "acute" hemodynamic disturbances, physical and temperature discomfort, neuropsychological asthenization, vegetovascular dysfunction with deconditioning of the cardiovascular system for exercise and orthostatic factors, statokinetic disturbances, metabolic-endocrine, neuromuscular and trophic disorders, nociceptive syndrome and others.

Table 1.
Dynamics of diastolic blood pressure (mm Hg) in central retinal artery (M±m)

Examination day	Group of subjects		
	1	2	3 (control)
Background	34±1	31±1	33±1
AOH:			
2	45±1	48±1	46±2
5	49±1	43±2	46±1
10	41±1	47±2	49±1
21	44±1	42±2	45±2
31	42±1	48±1	38±1
61	40±1	41±1	41±2
93	46±1	45±2	46±1
121	50±1	48±2	45±2
148	48±1	52±2	46±1
177	44±2	51±2	48±2
Recovery period:			
4	45±1	46±1	47±1
8	47±1	51±1	46±2

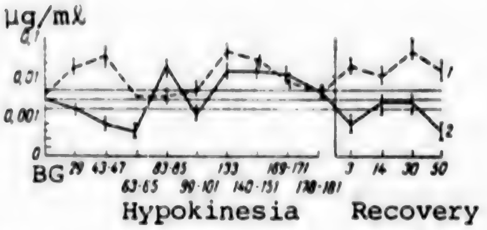
Development of the syndromes of "acute" hemodynamic disturbances, physical and temperature discomfort is attributable to the start of adaptation and reorganization of functional systems related to antiorthostatic position, redistribution of blood, restriction of customary amount of motor activity, etc. The clinical symptoms of the "acute" period of adaptation to prolonged AOH were analogous to those observed in previous studies involving briefer hypokinesia [1]. There were sensations of blood rushing to the head, dull headaches, which usually increased during the 1st day of hypokinesia. After a few hours there were the following objective findings: hyperemia of the face and neck, injected sclera and nasal congestion. On the 2d-3d day, we additionally observed puffiness of the face, narrowing of eye slits and smoothing of facial wrinkles. At this time, the subjects usually lay calmly and made limited (conservative) head movements. On the 3d day, against the background of some attenuation of the above symptoms, there were signs of physical and temperature discomfort: pain and unpleasant sensations in various parts of the body, chiefly in muscles of the neck, back, lumbar region, chilling and cooling of distal parts of the limbs, in spite of comfortable ambient temperature (22-23°C).

By the 8th-10th day, these signs of the "acute" period of adaptation to AOH disappeared almost entirely and the subjects had no complaints to the end of the first month. It should be stressed that the entire range of above-mentioned subjective symptoms was the most prominent in the third (control) group of subjects. At the start of the second month, there was differentiated development (earlier in the third group) of syndromes of vegetovascular dysfunction (VVD) and asthenization of the body, the signs of which progressively increased with increase in duration of AOH. Objectively, we also observed some neurological symptoms: nystagmoid twitching in extreme positions of the eyeballs, liveliness and asymmetry of tendon and periosteal reflexes (more often there were higher parameters on the right than on the left), inconsistently pathological Babinsky, Rossolimo, oral automatism reflexes, etc. There was progression of signs of muscular hypotrophy, hypotension and other trophic disorders (dryness of the integument and mucosa of the upper respiratory tract, friability and bleeding of gums, brittleness of the nails, exacerbation of parodontosis and others). Against such a background (more distinctly in the third group), we observed signs of the statokinetic syndrome: discoordination of static and motor acts, lack of accuracy and misses in performing demonstrative tests and locomotor acts, change in vestibular reaction, etc. Concurrently with the VVD syndrome, there was progression of signs of deconditioning of the cardiovascular system, which were more distinct in the functional tests.

The dynamics of circulatory parameters of the eye and intraocular pressure were characterized by development of stasis in the eye's venous system and compensatory elevation of blood pressure in the central retinal artery at the acute stage of adaptation to redistribution of blood during AOH. At some stages of hypokinesia, diastolic blood pressure in the central retinal artery remained elevated and did not return to the base level by the 8th day of the recovery period (Table 1).

Our study of parameters of lipid metabolism (Table 2) revealed a reliable increase in blood cholesterol esters, β-lipoproteins, decline of lecithin-cholesterol index, increase in cholesterol, etc. In the tests with 49-day AOH, we observed appearance of cholesterol precursors that are inherent in the early stages of atherosclerosis.

Examination of the adrenosympathetic system (ASS) and vagoinsular neuromediator activity of the autonomic nervous system (ANS) revealed fluctuating changes. Thus, throughout the test period catecholamine (epinephrine and norepinephrine) content of blood was above the mean normal levels, with the exception of the interval between the 65th and 100th days (see Figure). Acetylcholine (AC) level dropped already at the end of the 1st month and was below normal to the 65th day. In the middle of the study (90th-100th days), AC level was within the range of normal fluctuations, and in the second half of the study it rose and held at above the normal range to the end of AOH. The phasic reactions referable to ANS activity during prolonged hypokinesia were indicative of the fact that adaptation processes involve certain difficulties under hypokinetic conditions.



Dynamics of levels of catecholamines (1) and acetylcholine (2) in the course of the study. X-axis, day of examination; y-axis, quantitative parameters of tested hormones (µg/mℓ) BG) background

One of the subjects in the control group merits some attention: he developed severe vertigo upon moving the head on the 97th day of AOH, in the afternoon, following a routine exercise session; he examined objects with instability, presenting nausea, marked general weakness and hyperhidrosis. These signs became more intensive whenever he tried to change the position of his head. Objectively, there was elevation of arterial pressure to 145/100 mm Hg. His neurological status revealed horizontal nystagmus with the eyeballs in extreme positions, asymmetry of the nasolabial folds, deviation of the tongue to the left, some depression of tendon and periosteal reflexes, Babinsky symptom on the right, slight miss in the finger-to-nose test and hyperhidrosis. Eyegrounds revealed dilatation of retinal veins, accentuation of reflexes to light along the vascular bundle and peripapillary edema of the retina.

Approrpiate therapy was prescribed for this subject and he was excused from all types of conditioning. After 5 days, the fundus of the eye reverted to normal and by the end of the 3d week there was complete regression of the noted neurological changes. These signs were evaluated as transient impairment of cerebral circulation in the system of the basilar artery. The scheduled preventing conditioning was resumed on the 118th day, but started in a reduced volume with gradual increase to the required level within 2 weeks. It should be noted that the parameters of lipid metabolism presented greater change in this subject in the 2d and particularly 3d month of AOH than other subjects. Thus, lipoprotein content increased to 907 mg% and cholesterol to 250 mg% (versus 174 mg% in the base period). There was also elevation of parameters of fibrinolytic activity.

With regard to the dynamics of clinical disorders observed in our studies, it should be noted that the most distinct increase in severity of disorders in most systems was demonstrable up to the 90th-100th day, after which there was relative stabilization of the developed changes. The only exceptions were the asthenization and VVD syndromes, the severity of which continued to increase, though less distinctly than during the first half of the study.

Our studies revealed that some systems (autonomic and neuropsychological sphere, cardiovascular system, metabolic processes and in particular hormonal, fluid-electrolyte, lipid, etc.) are more sensitive to AOH factors, they develop changes earlier and the changes are more marked, whereas recovery is slower in the readaptation period.

Table 2. Dynamics of parameters of lipid metabolism in the control group (M±m)

Parameter	Mean base data	Days of AOH					Days of recovery period			
		26	46	86	136	178	1	5	14	28
Cholesterol, mg%	222	+25±26	+5±24	+17±16	+21±9,6	−6±17	−21±20,2	−42±13*	−29±17,8	−53±17,6
Free cholesterol, mg%	108	−17±6*	−3±9	−13±16	−51±9**	−47±6**	−30±11*	−9±10	−23±17	0±13
Cholesterol esters, mg%	110	+38±21	+9±16	+14±22	+69±9**	+57±27	+8±5	−30±14	−7±9	−38±18
Esterification index	0,5	+0,09±0,03*	+0,02±0,02	+0,09±0,07	+0,24±0,03**	+0,24±0,04**	+0,11±0,03*	−0,07±0,06	+0,06±0,06	−0,12±0,06
Lecithin, mg%	234	−8±15	−1±14	−38±16	−36±10*	−46±8**	−44±11**	−42±11*	−21±12	−19±9
Lecithin-cholesterol index	1,08	−0,1±0,07	0,01−0,12	−0,23±0,05**	−0,19±0,05*	−0,17±0,07	−0,03±0,04	−0,01±0,1	+0,07±0,04	+0,14±0,08
Kunkel test, units	27	+13±5	+12±4*	+9±3*	+7±5	+3±5	+1±3	+5±3	+4±3	+4±3
β-lipoproteins, mg%	630	−48±138	+412±134*	+306±114*	±304±92*	±267±82*	−8±121	−25±74	−102±121	+93±138
Cholesterol in β-lipoproteins,	163	+44±19	+5±29	+24±19	+35±12*	+19±19	−12±16	−40±13*	−49±19	−21±21

* $P<0,05$ **$P<0,001$.

Analogous findings were described by N. N. Gurovskiy and A. D. Yegorov [2] with reference to processes of adaptation to long-term weightlessness. These authors reported that, at the phase of completion of the main adaptive reactions, which lasts about 6 weeks, there was development and fixing of adaptive and compensatory reactions which appear to prevent progression of changes induced by weightlessness. This corresponded to the subjective evaluation of the cosmonauts, who stated retrospectively that "complete" adaptation to weightlessness during long-term space flights occurs in about the middle of the second month of flight.

There was relatively slow regression of changes caused by prolonged AOH. After some intensification of most disorders observed during hypokinesia (usually on the first few days) there was regression of clinical disturbances. The recovery processes following 182-day AOH occurred against a background of elevated ASS activity and diminished activity of the vagoinsular part of the ANS, which is indicative of strained adaptive mechanisms. The prolonged (2 or more months) recovery of clinicophysiological and metabolic-endocrine disturbances is indicative of the adverse effects of prolonged restriction of movement. The metabolic and hormonal disturbances associated with prolonged AOH, which were combined with other hypokinetic disorders (changes in tonus of the vascular wall, blood flow rate and blood viscosity) in the presence of vegetovascular disorders increase the risk of early development of atherosclerosis.

The changes that arise at the early stages of AOH are a reflection of consistent processes of adaptation to redistribution of blood and change in excitability of the reflexogenic regions of the chest and head. At later stages thereof, due to the prolonged strain of adaptive mechanisms, there is development of more complex changes in regulatory and effector systems, which could lead to disruption of the normal course of adaptive reactions, compensatory and defense mechanisms, as well as development of pathophysiological processes that require appropriate corrective measures in the recovery period.

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41/-06:613.27:546.18+615.356.577.161.22

EFFECTS OF 1α-HYDROXYCHOLECALCIFEROL AND DIFFERENT AMOUNTS OF PHOSPHORUS IN FOOD ALLOWANCE ON SOME PARAMETERS OF PHOSPHORUS AND CALCIUM METABOLISM IN HYPOKINETIC RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 26 May 81) pp 34-40

[Article by N. V. Blazheyevich, V. B. Spirichev, A. S. Ushakov, M. S. Belakovskiy, A. L. Pozdnyakov and I. N. Sergeyev]

[English abstract from source] The exposure of rats to hypokinesia and a phosphorus-enriched diet (Ca:P = 1:3) was accompanied by hypocalciemia, hyperphosphatemia, calcium losses from bones and formation of calcificates in the kidneys. The decrease of the phosphorus content in the diet (Ca:P = 1:0.5-1:1) prevented these disorders. The administration of $1\alpha OHD_3$ at a dose of 0.025 μg/day arrested hypokinesia-associated hypocalciemia and bone changes. The administration of $1\alpha OHD_3$ together with a high phosphorus consumption enhanced nephrolithiasis and induced aortal mediacalcinosis in hypokinetic rats. These data indicate that phosphorus consumption should be reduced in order to prevent disorders in phosphorus-calcium metabolism during hypokinesia. They also suggest that administration of $1\alpha OHD_3$ may be hazardous in the case of excessive phosphorus consumption.

[Text] A change in phosphorus and calcium metabolism, manifested by increased elimination of calcium and phosphorus, hypocalcemia, skeletal demineralization and calcifications in soft tissues are among the adverse consequences of exposure to hypokinesia [1, 2].

Optimization of calcium and phosphorus intake in food could be one of the means of preventing these disturbances. The proportion thereof in the diet of modern man is often other than the recommended level, and it is shifted in the direction of excessive phosphorus intake. Thus, the proportion of calcium and phosphorus in the diet of the population of the United States constitutes an average of 1:2.8, while the recommended ratio in that country is 1:1 [3].

It was previously demonstrated that excessive phosphorus intake (Ca:P = 1:3) causes hyperphosphatemia, hypocalcemia, osteoporosis and calcinosis of soft tissues with predominant involvement of kidneys of intact rats [4], and that it accelerates development of analogous disturbances in animals with experimental chronic renal insufficiency [5]. On the other hand, reduction of phosphorus intake to a ratio of Ca:P = 1:0.5 prevents development of these disturbances to a considerable extent [5].

For this reason, it was interesting to examine the effects of different amounts of phosphorus in the diet (Ca:P = 1:0.5, 1:1 and 1:3) on the state of phosphorus and calcium metabolism under experimental hypokinetic conditions.

The active metabolites of vitamin D, in particular, 1,25-dioxycholecalciferol, which is responsible for intensification of calcium and phosphorus absorption in the intestine, maintenance of normal calcium concentration in blood and remodeling of bone tissue, play an important part in regulation of calcium and phosphorus metabolism.

We therefore investigated the possibility of correcting disturbances in phosphorus and calcium metabolism under hypokinetic conditions by means of administration of 1α-hydroxycholecalciferol ($1\alpha OHD_3$)--a synthetic analogue of 1,25-dioxycholecalciferol with similar biological activity--to animals.

Methods

Experiments were conducted on male August rats weighing 200 g. The animals were separated into three groups and kept on a semisynthetic diet, the composition of which was described previously [6]. The calcium content in the food allowance of all groups was the same and constituted 0.6%. Phosphorus content in the diet constituted 0.3% in the first group of animals, 0.6% in the second and 1.8% in the third. Thus, the animals in these groups received a diet with calcium and phosphorus ratio of 1:0.5, 1:1 and 1:3, respectively. Each group was subdivided into four subgroups: the first consisted of control animals (with no restriction of movement), the second of animals kept under hypokinetic conditions, the third of animals under hypokinetic conditions given $1\alpha OHD_3$ throughout the experimental period, the fourth consisted of animals kept under hypokinetic conditions and given $1\alpha OHD_3$ for 15 days at the end of the experiment.

To create hypokinetic conditions, the animals were kept in small cages that restricted motor activity severely. They were kept in such cages for 70 days.

$1\alpha OHD_3$, which was kindly provided by N. A. Bogoslovskiy, was given to the rats daily in a dosage of 0.025 μg in 0.1 mℓ propylene glycol, by mouth. This dosage is considered physiological for rats [7].

In the course of the experiment we determined the concentration of calcium and phosphorus in blood serum, as well as daily excretion of these elements and hydroxyproline in urine [8-10]. The tests were made twice, on the 20th and 70th days of hypokinesia. In addition, when the animals were sacrificed at the end of the experiment, we assayed calcium and phosphorus in the aorta and kidneys [11]. We determined the specific weight of femoral diaphyses, as well as calcium, phosphorus and hydroxyproline levels in them in order to evaluate the changes in bone tissue [7].

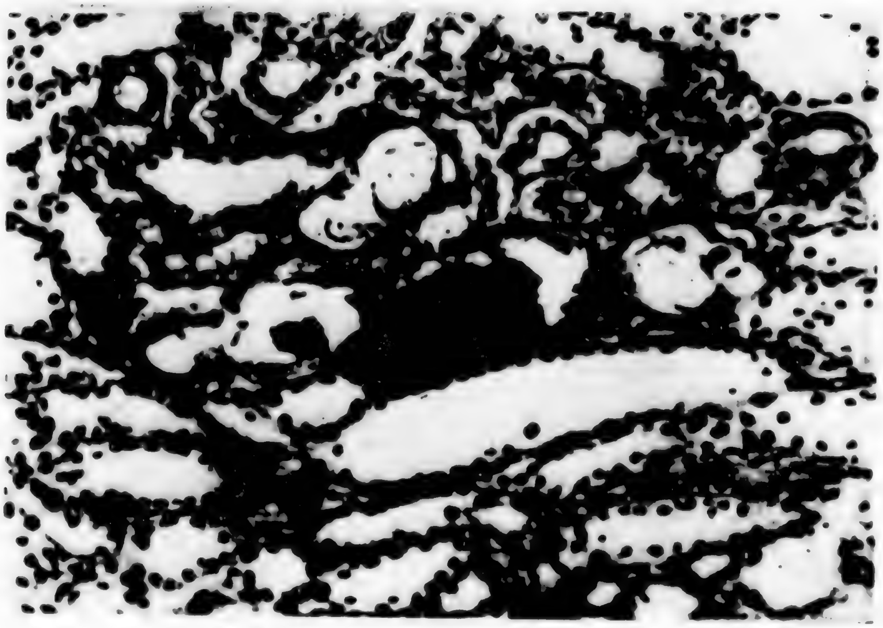

Figure 1. Microliths in kidney of rats kept on diet with Ca:P ratio of 1:3 for 70 days under hypokinetic conditions. Hematoxylin-eosin stain; magnification 200×.

We conducted a histological examination of tissues of the kidneys, heart, lungs, liver, spleen, mesentery lymph nodes and aorta. Pieces of the latter were taken from the thoracic region on the level of the arch and abdominal region on the level of the bifurcation. Material taken immediately after sacrificing the animals was fixed in 10% formalin and Carnoy fluid, then imbedded in paraffin. Sections were stained with hematoxylin and eosin, as well as picrofuchsin according to van Gieson. For demonstration of calcium the material was treated according to Koss, for demonstration of elastin it was treated with fuchselin according to Weigert, for lipids it was stained with sudan III+IV according to Goldman and oil red, for demonstration of acid mucopolysaccharides it was stained with alcian blue according to (Stidman), as well as toluidine blue at pH 7.0 and 4.0 with preliminary treatment of part of the sections with methyl alcohol for 2 h; for demonstration of neutral mucopolysaccharides the material was treated according to Shabadash and for RNA by the method of Brachet.

Results and Discussion

Table 1 lists data on levels of calcium and phosphorus in blood serum of experimental animals. An increase in phosphorus content of the diet to a Ca:P ratio of 1.3 elicited some decrease in calcium concentration of blood of control animals, which is consistent with previous findings [5, 12]. There was more marked decline of this parameter under hypokinetic conditions in this group of animals. Administration of 1αOHD$_3$ prevented the decrease in concentration of blood serum calcium in these animals. With a calcium/phosphorus ratio of 1:0.5 and 1:1, hypokinesia did not elicit reliable change in concentration of serum calcium. Under these conditions, 1αOHD$_3$ did not affect the parameter under study. The changes in calcium concentration in experimental animals were the same on the 20th and 70th days of the experiment.

Table 1. Effect of 1αOHD$_3$ on blood serum calcium and phosphorus content in animals kept on diets differing in proportion of these elements under hypokinetic conditions (M±m)

Animal group	Ca:P in diet	Calcium, mg/100 mℓ		Phosphorus, mg/100 mℓ	
		day of experiment			
		20	70	20	70
Control	1:0,5	9,1±0,1 (8)	9,5±0,2 (8)	8,6±1,2 (8)	6,8±0,6 (8)
	1:1	9,1±0,1 (11)	9,7±0,3 (13)	7,3±0,6 (11)	7,2±0,4 (14)
	1:3	8,7±0,1 (8)	8,9±0,1 (6)	8,2±0,8 (8)	6,6±0,5 (6)
		$P_1<0,02$	$P_1<0,01$		
Hypokinesia	1:05	9,1±0,2 (8)	9,3±0,3 (7)	7,6±0,8 (8)	6,1±0,3 (7)
	1:1	8,8±0,2 (11)	9,5±0,5 (14)	7 4±0,6 (11)	8,0±0,4 (14)
	1:3	7,5±0,4 (8)	7,8±0,6 (7)	12,1±1,5 (8)	10,2±3,6 (6)
		$P_1<0,01$ $P_2<0,01$	$P_1<0,05$	$P_1<0,02$	
Hypokinesia + 1αOHD$_3$	1:0,5	9,5±0,2 (8)	9,4±0,3 (8)	7,5±0,7 (8)	6,8±0,4 (8)
	1:1	8,9±0,2 (11)	9,2±0,2 (13)	7,7±0,7 (11)	7,8±0,5 (13)
	1:3	8,6±0,2 (8)	8,8±0,3 (5)	10,1±1,5 (8)	9,5±2,7 (5)
		$P_1<0,01$ $P_3<0,05$			
Hypokinesia + 1αOHD$_3$ for last 15 days prior to sacrificing animals	1:05		8,6±0,6 (8)		7,0±0,6 (8)
	1:1		9,3±0,6 (8)		6,5±0,8 (7)
	1:3		9,1±0,2 (8)		7,3±0,9 (8)

parentheses.

P_1) reliability of differences from control group given diet with Ca:P = 1:1

P_2) reliability of differences from corresponding group of control animals given diet with the same Ca and P ratio

P_3) reliability of differences from corresponding group of animals submitted to hypokinesia and on a diet with the same Ca:P ratio

There was no change in blood serum phosphorus concentration in control animals when the amount of this element in their diet was changed. Under hypokinetic conditions, animals given a diet with excessive phosphorus presented an increase in concentration thereof in blood serum. 1αOHD$_3$ had no appreciable effect on blood phosphorus content in experimental animals.

Table 2 lists data on excretion of calcium and phosphorus in urine of experimental animals. On the 20th day of the study, calcium excretion in urine was the same in all groups of animals, regardless of phosphorus content in their diet, hypokinesia and administration of $1\alpha\mathrm{OHD}_3$, for which reason these data are not listed in the table. On the 70th day of the experiment, we observed a tendency toward increase in calcium excretion in urine of rats submitted to hypokinesia and given excessive phosphorus plus $1\alpha\mathrm{OHD}_3$. However, this increase was statistically unreliable because of the wide scatter and small number of individual readings.

Table 2. Effect of $1\alpha\mathrm{OHD}_3$ on calcium and phosphorus excretion in urine of hypokinetic animals on diets differing in proportion of these elements on 70th experimental day (M±m).

Animal group	Ca:P in diet	Ca, mg/day	P, mg/day
Control	1:0.5 (5) 1:1 (5) 1:3 (5)	0.22 ± 0.05 0.20 ± 0.05 0.25 ± 0.03	9.0 ± 2.2 10.3 ± 5.8 26.0 ± 5.4 $P_1 < 0.01$
Hypokinesia	1:0.5 (5) 1:1 (6) 1:3 (6)	0.17 ± 0.04 0.19 ± 0.04 0.17 ± 0.02	12.7 ± 3.6 9.9 ± 3.4 32.9 ± 3.3 $P_1 < 0.01$
Hypokinesia + $1\alpha\mathrm{OHD}_3$	1:0.5 (6) 1:1 (6) 1:3 (5)	0.13 ± 0.06 0.14 ± 0.02 0.42 ± 0.14 $P_2 > 0.05$ $P_3 > 0.05$	9.2 ± 2.2 12.5 ± 1.5 21.9 ± 3.6 $P_2 < 0.01$ $P_3 < 0.05$
Hypokinesia + $1\alpha\mathrm{OHD}_3$ for last 15 days prior to sacrificing animals	1:0.5 (6) 1:1 (6) 1:3 (6)	0.17 ± 0.04 0.17 ± 0.02 0.22 ± 0.07	10.0 ± 2.0 10.9 ± 1.0 28.5 ± 10.8 $P_1 < 0.01$

Phosphorus excretion was 2-3 times greater in all animals given excessive amounts of this element in their diet (Ca:P = 1:3). This increase was observed on both the 20th and 70th experimental days, so that Table 2 lists only data referable to the second analysis. Administration of $1\alpha\mathrm{OHD}_3$ diminished somewhat excretion of phosphorus in rats submitted to hypokinesia and given an excess of this element ($P<0.01$).

There was no appreciable change in hydroxyproline excretion in experimental animals.

Data on calcium content in the kidneys and aorta of experimental animals are listed in Table 3. Keeping rats on a diet with excessive phosphorus (Ca:P = 1:3) led to renal calcinosis in all subgroups, and this is consistent with previous findings [4, 12]. Histological examination revealed numerous deposits of phosphorus and calcium salts in the form of microliths of different sizes (Figure 1) in the kidneys, on the boundary between the medullary and cortical substance, in the lumen of collecting tubules and distal segments of convoluted tubules. The larger ones caused total or partial obturation of the tubular lumen, producing in some areas considerable dilatation of overlying tubular segments. In the areas of localization of microliths, the tubular epithelium underwent necrobiotic changes or was desquamated. In the latter instances, the tubular walls were represented only by severely thickened basilar membranes. In some cases the tubular walls, which merged with nicroliths, became indistinguishible. Tubules containing no microliths were generally unchanged. Atrophic epithelial changes were observed only in the severely dilated segments of tubules without microliths. The lumen of such tubules was empty, less often filled with friable, shapeless material with mildly positive reactions for RNA, acid and particularly neutral mucopolysaccharides.

Table 3. Effect of $1\alpha OHD_3$ and diets differing in calcium/phosphorus on calcium content of kidneys and aorta of hypokinetic animals (in mg/g dry tissue; M±m)

Animal group	Ca:P in diet	Kidney	Aorta
Control	1:0,5 (7) 1:1 (14) 1:3 (8)	0,9±0,1 1,2±0,2 12,2±2,3 $P_1<0,001$	1,6±0,3 1,7±0,2 1,6±0,2
Hypokinesia	1:0,5 (7) 1:1 (14) 1:3 (8)	0,8±0,1 1,0±0,1 13,4±1,4 $P_1<0,001$	1,5±0,3 1,7±0,2 1,5±0,1
Hypokinesia + $1\alpha OHD_3$	1:0,5 (8) 1:1 (13) 1:3 (7)	1,4±0,4 1,2±0,2 16,5±3,2 $P_1<0,001$	1,7±0,2 1,7±0,3 2,6±0,8*
Hypokinesia + $1\alpha OHD_3$ for last 15 days prior to sacrificing animals	1:0,5 (8) 1:1 (8) 1:3 (8)	0,9±0,1 1,0±0,2 13,1±1,4 $P_1<0,001$	1,2±0,1 1,2±0,2 2,4±0,4 $P_1<0,01$

*Calcium concentration in the aorta constituted more than 2.0 mg/g dry tissue in 5 out of 7 animals in this group.

Prolonged intake of $1\alpha OHD_3$ under hypokinetic conditions caused somewhat greater accumulation of calcium in the kidneys and more marked morphological changes in them in animals given excessive amounts of phosphorus. There was histological demonstration of small microliths in the kidneys in isolated instances among animals given $1\alpha OHD_3$ throughout the experiment and kept on a diet with balanced calcium and phosphorus content (Ca:P = 1:1 and 1:0.5).

Use of $1\alpha OHD_3$ also elicited some increase in calcium content of the aorta in part of the animals on a diet with excessive amounts of phosphorus, which is indicative of development of calcinosis of the aorta. Histologically, these animals presented calcium deposits in the aorta in the region of the intima and inner third of the media (Figure 2). These deposits were intensively stained with hematoxylin and Koss stain, and they were most often demonstrable in the form of different sized nidi. Less often (mainly in the abdominal aorta) calcium salts in the form of granular masses saturated diffusely the entire thickness of the media; however, in these cases too, most of the calcium, which formed focal accumulations differing in shape and size, was localized in the internal third of the media, near the intima or directly along its course. Staining for demonstration of elastin revealed an altered appearance of elastic fibers of such tunics, as well as of the internal layers of the media. They were irregularly swollen, dark or light brown in color; some were unraveled and in some places there were typical club-shaped thickenings alternating with thinned segments of fibers. There were accumulations of neutral and acid mucopolysaccharides in the areas of calcinosis and destruction of elastic fibers.

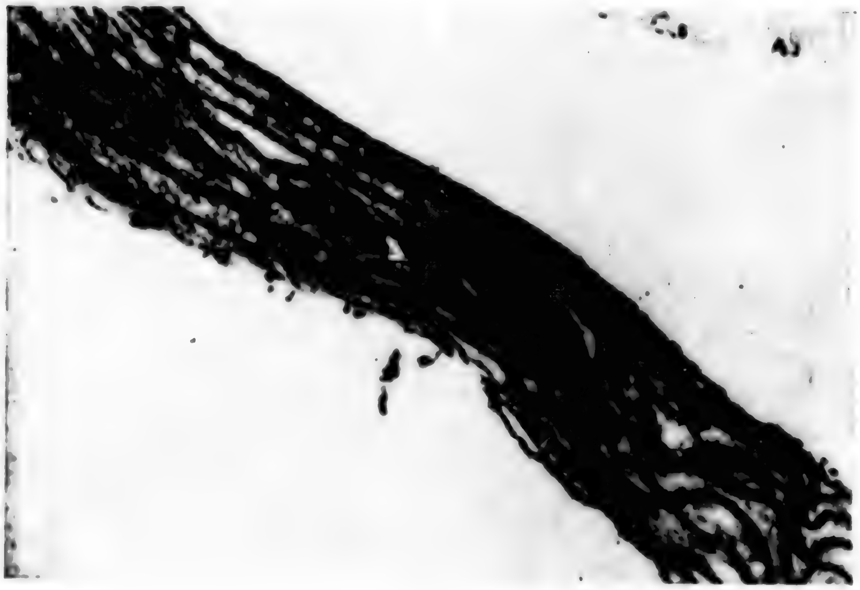

Figure 2. Calcinosis of aortic media in rats kept under hypokinetic conditions and on a diet with Ca:P = 1:3 for 70 days, given 1αOHD$_3$ throughout the experiment. Koss stain; magnification 200×

The demonstrated intensification of renal calcifications and development of calcinosis of the aorta with administration of physiological doses of 1αOHD$_3$ under hypokinetic conditions, against a background of excessive phosphorus intake, is consistent with analogous results of using this agent in the presence of experimental chronic renal insufficiency [6].

Hypokinesia did not elicit accumulation of calcium in soft tissues of animals on a diet with balanced calcium and phosphorus content, and it did not intensify renal calcinosis in animals kept on a diet with Ca:P = 1:3.

Table 4 lists data on the state of bone tissue of experimental animals. The specific weight of femoral diaphyses of experimental animals did not undergo reliable change under the influence of any of the factors used. We merely noted a tendency toward decrease in specific weight of bones of rats submitted to hypokinesia and given excessive phosphorus.

Table 4. Effect of $1\alpha OHD_3$ and diets with different Ca/P ratios on specific weight and chemical composition of femoral diaphyses in hypokinetic rats (M±m)

Animal group	Ca:P in diet	Specific weight	Calcium, mg/cm^3	Phosphorus mg/cm^3	Hydroxy-proline, mg/g dry tissue
Control	1:0,5 (8)	1,76±0,05	440±20	221±20	21±0,7
	1:1 (13)	1,76±0,02	461±17	209±5	22±2
	1:3 (8)	1,67±0,04	427±22	204±7	21±1
Hypokinesia	1:05 (7)	1,78±0,03	471±15	217±10	21±1
	1:1 (14)	1,73±0,04	450±15	215±4	22±0,8
	1:3 (8)	1,66±0 05	406±15	192±10	21±1
		$P_1>0,05<0,1$	$P_1<0,02$	$P_1<0,1>0,05$	
Hypokinesia + $1\alpha OHD_3$	1:0,5 (8)	1,68±0,05	416±35	198±9	22±1
	1:1 (13)	1,72±0,03	448±19	205±5	22±0,4
	1:3 (7)	1,68±0,03	440±24	211±6	21±0,7
Hypokinesia + $1\alpha OHD_3$ for last 15 days prior to sacrificing animals	1:0,5 (8)	1,72±0,04	418±14	207±9	20±0,4
	1:1 (8)	1,77±0,03	451±14	211±5	24±3
	1:3 (8)	1,67±0,03	412±21	199±8	20±0,7

There was also no appreciable change in calcium and phosphorus content of bones, with the exception of cases where the animals were submitted to hypokinesia and given a diet with excessive amounts of phosphorus. In this group of animals, we demonstrated a reliable decrease in calcium content and tendency toward decrease in phosphorus content of osseous tissue. Such changes were not found in animals kept under the same conditions, but given $1\alpha OHD_3$.

Thus, under our experimental conditions, hypokinesia did not elicit any changes in the parameters under study in animals given a diet with calcium/phosphorus ratio of 1:1 and 1:0.5. At the same time, hypokinesia aggravated disturbances referable to phosphorus-calcium metabolism that developed with a diet containing excessive phosphorus. The combination of hypokinesia and excessive phosphorus intake led to a decrease on mineralization of osseous tissue. These findings indicate that excessive (1.8%) intake of phosphorus could be an important factor that aggravates the effect of hypokinesia on phosphorus and calcium metabolism. This indicates that it is necessary to strictly maintain the calcium/phosphorus ratio in the diet from 1:0.5 to 1:1 under hypokinetic conditions, which is optimum for such conditions.

Administration of physiological doses of $1\alpha OHD_3$ throughout the experiment and for the last 15 days prior to sacrificing the animals prevented development of hypocalcemia and demineralization of bone tissue of hypokinetic animals given excessive amounts of phosphorus, and this could be indicative of the desirability of using this agent in combined prevention and therapy of disturbances in mineral metabolism under hypokinetic conditions.

However, the mild nature of hypokinesia and disturbances of phosphorus and calcium metabolism in rats given calcium and phosphorus in the optimum proportion (1:1) did not enable us to assess in this experiment the efficacy of $1\alpha OHD_3$ in preventing phosphorus and calcium metabolism disturbances that developed in the case of deep and prolonged hypokinesia, in spite of balanced calcium and phosphorus content in the diet [1, 2].

Our findings indicate that it is imperative to work out diets with optimum calcium/phosphorus ratio (Ca:P = 1:0.5-1:1) for hypokinetic conditions, and to develop appropriate foods.

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INFLUENCE OF LEVEL OF MINERALIZATION OF DESALINATED, HIGH QUALITY WATER OF THE HYDROCARBONATE CLASS ON FUNCTIONAL STATE OF MALE WHITE RAT GONADS

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[Article by O. I. Balashov, A. B. Sysoyev and A. V. Rodnikov]

[English abstract from source] As known, the salt content in the potable water has a gonadotropic effect, the level of which being in agreement with the traditional norm. However, within the normal limits one can distinguish better or worse functional manifestations. It has been shown that statistical treatment of the data, using the Student t-test, is of low efficiency because it neglects the ratio between groups. Of greater efficiency is the statistical treatment based on the domineering order. Proceeding from the theoretical speculations and experimental results, potable water with the mineral content of 250 mg/ℓ should be regarded as optimal.

[Text] Exploration of new geographic regions where there is no potable water, as well as the discovery of unique habitats, raised the question of recovering drinking water artificially. One of the popular methods of recovering potable water is distillation. However, experience has shown that both an insufficient and excessive level of mineralization of drinking water elicits a number of adverse physiological manifestations [1-5].

Determination of optimum mineralization level is an important hygienic direction of furnishing spacecraft and ship crews with desalinated potable water that meets the quality standard [6-10].

Recovery of optimum potable water implies that there is a specific list of physiological manifestations, on the basis of which the quality of a variant is determined.

It was previously shown that artificially produced potable water of the hydrocarbonate class of optimum quality, with mineralization levels of 250 and 500 mg/ℓ is the optimum according to parameters of energy and fluid-electrolyte metabolism [11]. Our main objectives here were to test the effects of different levels of mineralization of desalinated, standardized [good quality] potable water of the hydrocarbonate class on gonad function of male albino rats drinking such water for long periods of time and to select a criterion for evaluating results, which would enable us to unequivocally identify the best water. If the level of salts is below the optimum but in a range that does not strain compensatory capabilities of an organism, the problem is simply unresolved with regard to our initial goal. If the level of mineralization of drinking water is above the optimum, in addition to the fact that the problem is not solved in the physiological and hygienic respect, there is also an economically unfavorable factor in view of the unwarranted excessive use of salt supplements in preparing quality standard water artificially. For this reason, in determining the optimum level of mineralization of water we must introduce economic criteria, in addition to physiological ones. Proceeding from the need to coordinate the first and second requirements (concordance of hygienic and economic factors), the criterion for assessing mineralization level can be formulated as follows: one should achieve the best physiological manifestations related to the effects of water with minimum outlay of mineral salts to prepare potable water.

The dual nature of the criterion of optimum salt level in drinking water imposes greater requirements with regard to elaboration of quality, and makes it necessary to define the level according to both integral parameters of physiological functions and the various individual physiological systems.

The optimality criterion extends only to the category of water that is allowed by the current quality standard, and it is more specific under conditions where the capabilities of technological systems permit varying the quality readily within the limits of the current GOST. If the salt composition quantitatively meets the GOST requirements and is known to be good, one can pose the question of whether it is feasible to single out the best variant within the standard range according to physiological manifestations. But this best variant according to physiological evaluation must also take into consideration the social aspects, i.e., it should provide for optimum physiological functions with minimum outlay of materials.

Methods

A 7-month experiment was conducted on male white rats initially weighing 120-140 g, who were kept on a standard synthetic diet recommended by the Institute of Nutrition, USSR Academy of Medical Sciences. The animals were divided into 6 groups, each of which was given drinking water of a specific composition: distilled and with total mineralization of 50, 100, 250, 500 and 1000 mg/ℓ. The water was prepared by a previously developed method [12]. At the present time, this method has been introduced into practice, and the industry produces TU-6-09-3457-78 salt supplements, from which potable water is processed on ships, and its mineralization constitutes 500 mg/ℓ.

The animals were sacrificed after 7 months, and determination was made of mitotic activity of spermatogenic epithelium, size and relative weight of testes, relative weight of appendages, seminal vesicles and prostate. Motility of spermatozoa was measured; determination was made of their resistance to sodium chloride solutions, as well as resistance to acid [13]. We demonstrated some of the testicular enzymes involved in the key elements of one of the main forms of energy metabolism--Krebs cycle: lactate. pyruvate, isocitrate, α-ketoglutarate and succinate dehydrogenases [14]. The results were processed by statistical methods using the Student criterion and method of pair comparisons.

Results and Discussion

We failed to demonstrate clearcut patterns, according to parameters of activity of Krebs cycle enzymes, that would enable us to characterize the statistical significance of effects of mineralization levels in the tested water samples. Conversely, there was informative value in the parameters of activity of spermatozoa, their acid and osmotic resistance, motility and testicular weight coefficient.

Table 1 lists parameters that permit determination of the best water. We used the maximum value of the parameter of each series studied as an invariant value, in relation to which we calculated the degree of statistical difference according to Student's criterion. We proceeded from the following theoretical premises. If it is found that, in the course of evolutionary selection, that some individuals have a feature that makes them superior to other specimens, animals will accumulate in the population that will have expressly this advantage and in time they will be predominant in the population. In the case of natural selection, this will be manifested by differences in fertility. The initial thesis was substantiated by Rozen [17], on the principle of optimum design [18]. These theses logically ensue from the general criterion of biological optimum [19].

Analysis of the results listed in Table 1 shows that physiological manifestations correspond to the best variant the most often in animal groups given water with 500 mg/ℓ mineralization. It should be noted that the levels of manifestations are in the range of conventional parameters of the norm [20], with the exception of spermatozoal activity. Although for water with optimum mineralization a value of 500 mg/ℓ does not differ from the norm with statistical significance, this difference is quite substantial for water with other levels of mineralization. One should search for the reason for this in that measurement of activity is made visually, and it is based on a subjective evaluation, which is not sufficiently formalized.

But while parameters of functional manifestations in the group given water with mineralization of 500 mg/ℓ overtly dominate over others in frequency of manifestation of the maximum, it is not so simple to determine which group is closest to it or is an intermediate one with such classification of parameters. This is related to the fact that if we consider only the frequency of manifestation, we do not take into consideration its correlation to parameters in adjacent groups, and the latter procedure is the main one for decision making and ranking alternatives. Thus, the difference between parameters of animal groups does not allow us to demonstrate the qualitative aspect of the pattern, while the existing set of comparisons requires a special classification, in which the parameters will be the comparative correlations between them, rather than the values themselves. For this reason, we used a different method of classifying results at the next stage of our study, in which the parameters of each feature were arranged in order of preference. For example, for the parameter of spermatozoal "acid resistance," the ranking according to the adopted criterion of optimality should be given in the following form: 50 mg/ℓ>500 mg/ℓ>0 mg/ℓ>250 mg/ℓ>1000 mg/ℓ>100 mg/ℓ. The symbol > means that water with mineralization level of 50 mg/ℓ is preferable to water with 500 mg/ℓ salt, which, in turn, is preferable to distilled water, etc. Such classification has the property of transitivity [21], i.e., if it is stated, as in the example of acid resistance, that 50 mg/ℓ>500 mg/ℓ and 500 mg/ℓ>0 mg/ℓ, then 50 mg/ℓ>0 mg/ . For this reason, we can separate this ranking into elementary comparisons: 50 mg/ℓ>500 mg/ℓ; 50 mg/ℓ>0 mg/ℓ; 50 mg/ℓ>250 mg/ℓ; 50 mg/ℓ>1000 mg/ℓ; 500 mg/ℓ>0 mg/ℓ, etc. [22]. In all, we obtain 15 elementary comparisons for each parameter. Table 2 lists the final results of calculating them for each group. The extreme left column of the top line shows the level of mineralization of the tested water samples. The number of preferences is given at the intersection of each box. Thus, in 2 cases the functional manifestations in the group of animals given water with 50 mg/ℓ mineral salts were preferable to the parameters of the animal group given distilled water and in 1 case preferable to the parameters of animals given water with mineralization of 100 mg/ℓ, etc. The total number of preferences is given in the last column. In 22 cases, the functional manifestations in the group given water with mineralization level of 500 mg/ℓ were preferable to the parameters of other groups. In the group of animals given water with 250 mg/ℓ minerals, the total number of preferences constituted 14, etc. We can rank the levels of mineralization of the tested water samples in order of preference on the basis of these results: 500 mg/ℓ>250 mg/ℓ>100 mg/ℓ>distilled water>50 mg/ℓ>1000 mg/ℓ. According to the general criterion of equivalence [16], the frequency of optimum manifestations was higher, with statistical reliability, in the group of animals given water with 500 mg/ℓ minerals, with a significance level of 5%, than in animals given water with other amounts of minerals. The value of χ^2 with 5 degrees of freedom and 5% level of significance is 11.07, while the general criterion of equivalence is 18.6 (18.6>11.07). Thus, a salt level of 500 mg/ℓ is referable to the optimum variant of mineralization. But if we refer to the optimality criterion, which was adopted, it is necessary for this mineralization level to be the lowest of possible levels. We find by the method of contrasts [16] that the statistical difference between optimum numbers of functional manifestations in groups of animals given water with 250 and 500 mg/ℓ minerals is unreliable. At the same time, the difference in optimum frequency of functional manifestations between other groups was reliable.

Consequently, potable water with mineralization level of 250 mg/ℓ meets the optimum requirements.

Thus, the level of mineralization of potable water has a gonadotropic effect, though it is mild. The functional manifestations conform to the norm. However, one can single out manifestations within the normal range that are the best in a certain sense.

Since the active factor is referable to low-intensity factors, statistical processing using the Student criterion is not always effective. In order to determine the preferable level of mineralization, one must resort to ranking alternatives and, on the basis of elementary preferences, determine the dominant series of functional manifestations.

Table 1. Some parameters of spermatogenesis, functional state of gonads and spermatozoa of white rats given water containing different amounts of minerals, M±m

Parameter	Distilled water	Hydrocarbonate water with mineralization levels of (mg/ℓ)				
		50	100	250	500	1000
Activity of spermatozoa, arbitrary units	0,41±0,11 n=6; t=0,57	0,19±0,05 n=5; t=1,82	0,37±0,04 n=8; t=0,87	0,29±0,05 n=6; t=1,28	0,53±0,18 n=7	0,31±0,34 n=7; t=0,57
Acidity resistance, pH units	3,46±0,13 n=6; t=4,74	2,71±0,09 n=5	3,63±0,12 n=8; t=6,13	3,54±0,09 n=6; t=6,52	3,29±0,05 n=7; t=5,63	3,55±0,07 n=7; t=7,37
Osmotic resistance to sodium chloride solution, % solution	2,13±0,16 n=6; t=2,97	2,45±0,28 n=4; t=0,81	2,48±0,13 n=8; t=1,28	2,33±0,21 n=6; t=1,55	2,69±0,10 n=7	2,29±0,13 n=7; t=2,44
Sperm motility, min	265±24,5 n=6; t=4,07	213±11,0 n=5; t=7,97	286±23,1 n=8; t=3,52	372±34,0 n=6; t=0,53	393±19,8 n=7	348±15,5 n=7; t=1,80
Testicular weight coefficient, g/kg	8,30±0,18 n=6; t=2,29	8,25±0,24 n=5; t=2,23	8,63±0,18 n=8; t=1,43	9,18±0,34 n=6	8,36±0,24 n=7; t=1,97	8,28±0,23 n=7; t=2,19
Spermatogenesis index, arbitrary units	8,20±0,50 n=30; t=2,86	8,33±0,62* n=2,45	8,46±0,38 n=35; t=2,7	9,01±0,60 n=30; t=1,71	10,50±0,63 n=303	8,41±0,31 n=35; t=2,98

Note: The table lists mean values, standard errors, size of sample and Student coefficients calculated in relation to the optimum. The underlined figures correspond to the optimum for the series, according to the evaluation criterion used in this study. The asterisk notes the value obtained by estimation using the method of shortened ["truncated"] series.

Table 2. Number of elementary preferences and total thereof in paired comparisons of animal groups

Mineralization of tested water, mg/ℓ	0 mg/ℓ	50 mg/ℓ	100 mg/ℓ	250 mg/ℓ	500 mg/ℓ	1000 mg/ℓ	Total elementary preferences
0		3	2	2	0	3	10
50	2		1	2	1	2	8
100	3	4		2	1	3	13
250	3	3	3		1	4	14
500	5	4	4	4		5	22
1000	2	3	2	1	0		8

A mineral content of 500 mg/ℓ in potable water is desirable according to frequency of optimum manifestations. One should give preference to 250 mg/ℓ according to the optimality criterion adopted by us. There was a statistically unreliable difference between 500 and 250 mg/ℓ with respect to frequency of optimum manifestations.

The obtained data were used to set standards for mineral content of desalinated sea water.

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SOME PHYSIOLOGICAL AND BIOCHEMICAL FEATURES OF CELLS OF CARROT GALL DEVELOPED IN WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 7 Apr 81) pp 45-48

[Article by M. G. Tairbekov, L. A. Voronkov and N. A. Guzhova]

[English abstract from source] The paper presents the results of experiments with the carrot tissues infected with Agrobacterium tumefaciens flown onboard the biosatellite Cosmos-1129 in cooperation with the US scientists. Postflight, the respiratory activity of tumor cells was determined and K^+ and Na^+ permeability of cell membranes was measured. The resulting data give evidence that in weightlessness the development of the carrot gall tumor is accompanied by changes in the above physiological and biochemical parameters. The changes are, however, within the physiological limits, leading to no pathologies of the whole cell.

[Text] Experiments have been conducted on plants in spacecraft since the early 1960's. The vast majority of experiments with plants in weightlessness were concerned with investigation of their anatomical and morphological characteristics. At the same time, determination of the role of gravity in evolution of living organisms on earth is a basic task for space biology. The answer to this problem is apparently also related to investigation of cellular mechanisms of regulation of metabolic processes in weightlessness, which ultimately lead to adaptation of an organism to new living conditions. Information has been published in the literature to the effect that a change in gravity could be the cause of change in intracellular processes, in particular, intensity of respiration and photosynthesis [1-3], synthesis and breakdown of carbohydrates [4], qualitative and quantitative composition of enzymes [5-7]. Most of these data were obtained in laboratory experiments with the use of the clinostat, which is an instrument that is considered to simulate some of the effects of weightlessness.

An experiment with carrot tumor tissues infected with Agrobacterium tumefaciens, which was conducted aboard the Cosmos-1129 biosatellite together with U. S. specialists, is one of the few attempts at evaluating some parameters of functional activity of cells in weightlessness.

This experiment was proposed by Prof R. Baker and prepared under his supervision by a group of staff members in the department of botany and phytopathology of the University of Colorado, United States. In accordance with the program that was prepared in advance, the participation of Soviet specialists (Institute of Biomedical Problems, USSR Ministry of Health, and Moscow State University imeni Lomonosov) consisted of conducting the inflight and synchronous experiments, as well as postflight analysis of some of the data, namely, respiratory activity of tumor tissue and permeability of cell membranes to ions and electrolytes. In addition to the synchronous control experiment, transport, stationary and clinostat control experiments were conducted in the USSR and United States. The parameters of the transport control served as base data in all of the studies.

Methods

Plant material (carrot discs infected with Agrobacterium tumefaciens) were sent from the United States 6 days prior to the start of the experiment in a special transport incubator and stored at 4°C. The material was stowed on the biosatellite 2 days before lift-off, in special BB-2M containers, and exposed to weightlessness for 18.5 days at 24±1°C. The flight material was placed into the transport incubator directly at the spacecraft landing site in the field laboratory, and within 24 h it was delivered to the Laboratory of Physiology and Biochemistry of Phytopathogenic Microorganisms and Immunity, Department of Plant Physiology, Moscow State University, for postflight analysis. The gall tumor was carefully resected from carrot discs and weighed. In order to measure dry mass weight, the tissue was kept for 5 min at 105°C, then in an incubator at 60°C to a constant mass.

Respiratory activity was evaluated polarographically by means of a closed Clark electrode in a 2.7 mm^3 compartment in a medium containing 0.2 M potassium phosphate buffer, pH 7.4. The intensity of oxygen uptake was expressed in μM/g wet weight. The rate of oxygen uptake remained virtually constant throughout the period of taking readings, which was indicative of normal condition of tissues. A special unit was used to measure the rate of passage of electrolytes through the membrane. We assessed permeability of cell membranes for electrolytes according to change in specific electric conductivity of gall tissue extract. A batch of tissue was cut into 1.5 mm^3 pieces, placed in a nylon-6 [caprone] bag and washed in tap water for 30 min, then distilled for 3 min. The elution time was selected empirically in preliminary tests. In this time, injured metabolites and cell tissues are removed from the samples. After this, the material was placed in distilled water. In all of the measurements taken, there was a constant 1:10 ratio of the batch of tissue to water volume. After exposure to room temperature for 30 min, the extract was filtered and readings taken.

Flame photometry was used to measure K^+ and Na^+ ion content of gall tissue extracts.

Results and Discussion

The condition of the material was described immediately upon opening simultaneously all of the containers of the inflight and control experiments. Uniform and optimum growth of tumor tissue was observed in the flight experiment and in the dishes used in the transport and stationary control experiments. There was somewhat less mass and slower uniform growth of tissues in the clinostat control experiment. The only exception was the material in the synchronous control, where accumulation of dry mass was 30% less than in the transport control (Table 1). In addition, in all experimental variants there was better growth of gall tissue in the peripheral dishes in the container than in central ones, which can most probably be attributed to better aeration conditions in the container.

Table 1.
Accumulation of dry gall tissue mass of carrot

Experiment	Dry mass	
	mg/g wet mass	%
Transport control	97,96	100
Flight variant	109,06	111,3
Stationary control	92,47	94,4
Synchronous control	65,75	67,1
Clinostat	84,75	86,5

Table 2.
Respiratory activity of carrot tumor mass

Experiment	Respiratory activity			
	μM O_2/ g wet mass/ min	%	μM O_2/ g dry mass/ min	%
Transport control	$472 \cdot 10^{-3}$	100	$4819 \cdot 10^{-3}$	100
Flight variant	$420 \cdot 10^{-3}$	88,9	$3851 \cdot 10^{-3}$	79,9
Stationary control	$426 \cdot 10^{-3}$	90,2	$4605 \cdot 10^{-3}$	95,5
Synchronous control	$355 \cdot 10^{-3}$	75,2	$1399 \cdot 10^{-3}$	102,0
Clinostat	$552 \cdot 10^{-3}$	116,9	$6513 \cdot 10^{-3}$	135,1

Table 2 lists data referable to measurement of respiratory activity of tumor tissue. As seen in this table, the most intensive respiration was found in tumor cells that developed in the clinostat and the least intensive in those that were submitted to weightlessness. The results of the other control experiments were similar and occupied an intermediate position. This pattern was the most distinct when tumor tissue was scaled to dry mass (see Table 2).

An increase in respiratory rate of plants when rotated continuously on a clinostat was repeatedly observed and many authors attribute it to more uniform distribution of gravity-dependent cell elements over its entire volume as a consequence of active mixing of cytoplasm [1, 2]. These circumstances should lead to an appreciable decline of concentration gradients and, consequently, provide better conditions for interaction between cell organelles and the enzyme-substrate complex [8]. Moreover, it is known that movement of cytoplasm, which is an energy-dependent process inherent in virtually all types of cells, plays some part in the uniform distribution of cellular elements. Movement of cytoplasm does not stop in weightlessness, although the rate of this process is substantially lower than in the control. This was experimentally confirmed in an experiment with the lower fungus, Physarum policephalum, which was conducted aboard the same biosatellite. However, our measurement of respiratory activity in the clinostat indicates the opposite. Evidently, one should search for the cause of such inconsistency of results in the difference in physiological state of plant tissues in weightlessness and the clinostat. We refer, first of all, to "water stress," which occurs in plant tissues that develop in the clinostat due to intensive evaporation of water from the surface of the material. The cell responds to "water stress" by an increase in share of molecules, primarily the light carbohydrate fraction, which can retain water and prevent further drying of tissue. At the same time, the presence of relatively high concentration of oxidation substrate (light carbohydrates) leads to an increase in respiratory activity of the cell. An increase in proportion was demonstrated previously in the experiment with carrot gall conducted aboard the Cosmos-782 biosatellite [4].

Table 3.
Specific electric conductivity of carrot tumor tissue

Experiment	Specific electric conductivity	
	relat. units	%
Transport control	1,30	100
Flight variant	7,00	53,8
Stationary control	1,23	98,0
Clinostat	2,40	1,85

Table 4.
Concentration of K^+ and Na^+ ions in extract of carrot tumor tissue

Experiment	K^+ ion concentration		Na^+ ion concentration	
	mM/g dry mass	%	mM/g dry mass	%
Transport control	66,3	100	55,1	100
Flight variant	357,6	539	109,1	138
Stationary control	—	—	—	—
Synchronous control	85,3	129	77,6	141
Clinostat	113,3	171	44,6	80

Thus, in this experiment "water stress" was one of the substantial factors of increase in respiratory activity of specimens placed in the clinostat. Moreover, one should apparently not overlook the purely aerodynamic effect inherent in rotation in the clinostat, namely, disappearance of static microregions in the immediate vicinity of tissue, which facilitates access of oxygen to these regions.

In our opinion, these are the physiological bases of differences between experimental flight specimens and those used in the clinostat control experiment, with respect to respiratory activity of gall tissue. However, the above facts are not the only cause of low respiratory activity of gall tumor tissue in weightlessness, since the state of membranes plays a substantial part in these processes.

It is known that the membrane is the material basis, on the level of which are formed the different stages of the cell's reaction to environmental factors. There is sufficient information to conclude that the very earliest steps of the complicated mechanism of expression of the gravity stimulus perceived by the organism occur on the membrane level [10, 11]. For this reason, it was logically warranted to analyze the functional state of cell membranes, which was made in these studies, namely, determination of permeability thereof to electrolytes and K^+ and Na^+ ions. The results of these studies are listed in Tables 3 and 4.

On the basis of the data listed in Table 3, it can be concluded that there is almost 5.5-fold increase in passage of electrolytes from the cell into the environment under weightless conditions, as compared to the control, and 3 times greater than in the clinostat control experiment.

Assay of concentration of K^+ and Na^+ ions in tumor tissue extract revealed that there is a drastic increase in exit of K^+ from cells in weightlessness. This was also demonstrated for Na^+ with somewhat less marked difference (see Table 4). Unquestionably, these findings are indicative of increased permeability of cell membranes in weightlessness. Analogous findings were made in the joint Soviet-French experiment, "Cytos," which was performed with Paramecia aboard the Salyut-6 orbital station [12].

Thus, the postflight studies of some physiological and biochemical characteristics of carrot gall tumor cells lead us to conclude that development of cells in weightlessness is associated with changes in metabolic processes in them. Most probably, these changes are in the physiological range and do not lead to pathological impairment of structural integrity of the cell.

The relative stability of ultrastructural plant cells formed in weightlessness [13, 14] is indicative of the validity of the last hypothesis. The data submitted here, when compared to previously obtained results, confirm the assumption that weightlessness can be classified as a mild or moderate environmental factor, while the response manifested on the cellular level can be referred to the category of physiological adaptive reactions. Moreover, weightlessness apparently corresponds to a somewhat different model of distribution of cellular elements from what we observe in the clinostat. Consequently, rotation in the clinostat does not correspond, physiologically and biochemically, to the results of exposing living objects to weightlessness.

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FUNCTIONAL STATE OF RAT GASTROINTESTINAL TRACT ORGANS FOLLOWING FLIGHT IN COSMOS-1129 BIOSATELLITE

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[Article by K. V. Smirnov, L. G. Goland-Ruvinova, N. P. Goncharova, O. V. Zhiznevskaya, I. L. Medkova, N. M. Nikolayeva, R. A. Pechenkina and A. N. Petrusenko]

[English abstract from source] The enzyme-excretory and motor functions of the gastrointestinal tract of rats flown for 18.5 days onboard the biosatellite Cosmos-1129 were studied. Immediately postflight, the pepsin synthesis decreased and the dipeptide parietal hydrolysis increased. At R+6, the activity of the enzymes responsible for the cavitary and parietal hydrolysis of lipids significantly grew and that of the enzymes involved in protein hydrolysis fell. At R+30, the carbohydrate hydrolysis was inhibited and the activity of lipolytic enzymes enhanced markedly. The amplitude and rhythm of stomach biopotentials were dysbalanced. The so-called immobilization stress of intact rats brought about activation of lipase, monoglyceridyl lipase, dipeptidase and inhibition of amylase and invertase. The immobilization exposure of flight rats caused inhibition of the membrane hydrolysis of proteins and carbohydrates and lack of the pancreatic reaction.

[Text] Many facts have been accumulated to date that are indicative of changes in spectrum of digestive hydrolases in both man and animals during actual space flights [1, 2]. A comparison of the results of these studies to data obtained with simulation of such space flight factors as hypokinesia and accelerations made it possible to establish that weightlessness and hypokinesia play the leading role in these changes.

We have undertaken here the first attempt at a combined study of enzyme-secreting and peristaltic function of gastrointestinal organs of animals flown in the Cosmos-1129 biosatellite. Since some of the animals were submitted to immobilization stress after landing, it was possible to distinguish the changes related to the stress of weightlessness.

Methods

We used rats from a colony of Wistar SPF in the experiment. Animals flown in space for 18.5 days were decapitated 4-10 h after returning to earth (0 day), on the 6th and 30th day of the readaptation period, as well as after submitting them to immobilization stress on 0, 3d, 4th, 5th and 6th days after termination of the flight. Rats used in a synchronous experiment and in the vivarium control were decapitated at the same times.

The gastric mucosa, pancreatic tissue and small intestinal mucosa served as material for examination. Pepsin content of the gastric mucosa was assayed by the method of G. F. Korotko and M. E. Islyamova [3], pancreatic amylase and total amylolytic activity of the mucosa of the small intestine were determined by the method of Smith [4]. Activity of pancreatic lipase and monoglyceride lipase was determined by the method of I. L. Medkova et al. [5, 6]. Techniques that were modified by A. M. Ugolev et al. [7] were used to determine the activity of intestinal enzymes--invertase, glycyl-L-leucine dipeptidase. A 3GM-4M electrogastrograph was used to record bioelectric potentials of the stomach characterizing its peristaltic function. Gastrograms were processed by the method of Ya. S. Tsimmerman [8].

Results and Discussion

Proteolytic Enzymes

The animals presented a tendency toward decrease in pepsin content of a homogenate of gastric mucosa 4-10 h after the flight. The tendency toward depressed synthesis of this enzyme persisted on the 6th postflight day, and the decline in the group of animals used in the synchronous experiment was reliable ($P<0.02$). On the 30th day of the readaptation period, pepsin content of the gastric mucosa of the flight group of rats virtually failed to differ from the control, whereas synthesis of this enzyme was still low in the synchronous experiment rats (Table 1). In intact animals, immobilization stress led to reliable decrease in pepsin content of the gastric mucosa. The combination of immobilization and weightlessness elicited a reliable increase in pepsin secretion, as compared to the control group that was immobilized. We observed analogous, but less marked changes in the synchronous experiment (Table 2).

Examination of parietal hydrolysis of dipeptides in the small intestine 4-10 h after the flight revealed an increase in activity of glycyl-L-leucine dipeptidase in both the homogenate and on the surface of the mucosa. The changes were reliable in the proximal segment, which is apparently indicative of greater lability of the proximal parts of the intestine in weightlessness. Analogous, but less marked changes were observed in the synchronous experiment. On the 6th postflight day there was a tendency toward decrease in glycyl-L-leucine dipeptidase activity in the mucosa of the small intestine, whereas in the synchronous experiment there was also a change in proximodistal gradient of enzyme activity. On the 30th postflight day, there was drastic increase in glycyl-L-leucine dipeptidase activity in homogenates of the proximal and distal segments of the small intestine, whereas the activity of this enzyme was below the control level on the mucosal surface. In the synchronous experiment there was analogous distribution of glycyl-L-leucine dipeptidase activity in the small intestine. Immobilization stress elicited a tendency toward lowering of glycyl-L-leucine dipeptidase level both on the surface and in the homogenate of both segments of the small intestine. The combination of weightlessness and immobilization led to severe depression of glycyl-L-leucine dipeptidase activity on the surface of the proximal segment ($P<0.01$). In the synchronous experiment, we observed reliable changes in enzyme activity in the homogenate of proximal and distal segments of the small intestine.

Lipolytic Enzymes

As shown by the results of our studies, there was virtually no change in pancreatic lipase activity in pancreatic tissue of the group of rats decapitated 4-10 h after the flight and those used in the synchronous experiment; however, there was considerable (by more than 50%) increase in activity of this enzyme on the 6th postflight day ($P<0.05$). On the 30th postflight day, there was virtually no difference from control levels in activity of pancreatic lipase in pancreatic tissue (see Table 1). Immobilization stress led to a reliable increase in lipolytic activity of pancreatic tissue of rats in the vivarium control and synchronous experiment, as compared to intact animals. Immobilization had no effect on pancreatic lipase activity in animals flown in space (see Table 2).

During the first few postflight hours, there was virtually no change in pancreatic lipase activity of the small intestinal mucosa in either the flight group of animals or rats in the synchronous experiment; however, it increased very drastically and reliably on the 6th postflight day in both the proximal and distal segments. On the 30th day of the readaptation period, there was an increase in activity of this enzyme over the entire length of the intestine. Immobilization of intact animals led to drastic and reliable increase in activity of this enzyme in the mucosa of the small intestine, as compared to animals in the vivarium control.

There was reliable increase in lipolytic activity of the distal segment of the small intestinal mucosa in the groups of animals submitted to weightlessness and immobilization stress and rats in the synchronous experiment submitted to immobilization, as compared to the vivarium control.

With regard to the dynamics of changes in activity of monoglyceride lipase--the enzyme that completes hydrolysis of lipids on the surface of the intestinal epithelium--we can merely report some tendencies, since no reliable differences were demonstrable between control and experimental data in any of the experimental groups. There was negligible increase in activity of this enzyme, more so in the proximal segment, in rats decapitated 4-10 h after landing, as well as on the 6th postflight day. Activity of this enzyme virtually failed to differ from the control on the 30th postflight day. Immobilization stress elicited an increase in monoglyceride lipase in both the proximal and distal segments, as compared to intact animals.

Carbohydrases

There was some depression of amylase activity in pancreatic tissue 4-10 h after the flight. Conversely, we observed considerable increase in synthesis of

Table 1. Amylase and lipase content of pancreatic tissue and pepsin content of gastric mucosa

Group	Index	Postflight days								
		0 (4-10 h)			6			30		
		amylase	lipase	pepsin, mg%	amylase	lipase	pepsin, mg%	amylase	lipase	pepsin, mg%
		activity units			activity units			activity units		
Vivarium control	*M*	394 500	2740,5	1.46	324 000 000	2740.5	1.25	1 008 000	1753, 5	1.2
	±*m*	88 000	227,4	0,28	71 000 000	227.4	0,3	160 000	269,2	0.16
	n	6	10	7	6	10	6	5	5	5
Weightlessness	*M*	232 328	2632,5	1,06	302 000 000	5429.5	0,95	982 000	1680.0	1.44
	±*m*	18 950	299,3	0.3	72 800 000	505.9	0.26	183 000	151,3	0,07
	n	7	7	7	6	5	6	5	5	5
	P	>0.05	>0.5	>0,2	>0.5	<0,05	>0.2	>0.5	>0.5	>0.1
Synchronous experiment	*M*	503 400 000	2349,4	1,16	245 000 000	—	0,31	—	—	0,6
	±*m*	79 000 000	268,9	0.18	28 000 000	—	0,1	—	—	0,11
	n	7	6	7	6	—	5	—	—	5
	P	<0,001	>0.2	>0,2	>0.2	—	<0,02	—	—	<0.01

this enzyme (P<0.001) in the synchronous experiment. On the 6th postflight day, amylase activity of pancreatic tissue virtually failed to differ from control levels. Analogous findings were made in the synchronous experiment. On the 30th postflight day, there was normalization of amylase secretion according to most parameters, the only exception being a low amylase level in salivary glands. Immobilization stress elicited drastic decline in amylase activity of pancreatic tissue (P<0.001). However, in the group of animals submitted to weightlessness and immobilization the amylase level in the pancreas did not differ from the parameters for the intact control and flight groups. Analogous results were obtained in the synchronous experiment. Immobilization stress elicited depression of overall amylolytic activity of the small intestine. The combination of weightlessness and stress caused profound decrease of activity. Analogous, but less marked change was demonstrated in the synchronous experiment.

Studies of intestinal carbohydrase (invertase) activity failed to demonstrate changes in synthesis and translocation of this enzyme 4-10 h after the flight. We also failed to demonstrate any changes in carbohydrase on the 6th postflight day. Analogous findings were made in the synchronous experiment. On the 30th day of the readaptation period, invertase activity diminished reliably in the homogenate and on the surface of both segments of the small intestine (P<0.001). The same dynamics and severity of changes were inherent in the synchronous experiment. Immobilization stress elicited a depression of invertase activity in all parts of the small intestine, and it was the most marked in the homogenate of the proximal segment (P<0.001). The combination of weightlessness and stress had no effect on production and secretion of this enzyme on the mucosal surface of the small intestine.

Table 2. Amylase and lipase content of pancreatic tissue and pepsin content of gastric mucosa after immobilization stress

Group	Index	6th postflight day		
		amylase	lipase	pepsin
Vivarium control + immobilization	M	3 050 000	4296,4	0,54
	± m	680 000	365,2	0,1
	n	6	6	7
	P	< 0,01	< 0,001	< 0,001
Weightlessness + immobilization	M	367 280 000	2247,2	1,24
	± m	11 530 000	119,9	0,17
	n	7	5	7
	P	< 0,001	< 0,001	< 0,01
Synchronous experiment + immobilization	M	225 000 000	6097,5	0,76
	± m	30 000 000	1333,2	0,13
	n	7	7	7
	P	> 0,2	> 0,5	> 0,1

Peristaltic Function of the Stomach

Rats presented a decrease in amplitude of bioelectric potentials of the stomach, which reflect its contractile activity, 7-11 h after the flight. Analogous changes were noted in the synchronous experiment. In addition, we observed acceleration of rhythm of bioelectric potentials of the stomach both after the flight and after the synchronous experiment. The faster rhythm of gastric contractions must be interpreted as a process that compensates for the decline in amplitude of stomach contractions.

Thus, our study of digestive function in rats following an 18.5-day space flight established the following. In spite of the fact that the space flight did not generally elicit drastic changes in hydrolytic processes in the gastrointestinal tract, there was some tendency toward decrease in pepsin synthesis, which was associated with an increase in parietal hydrolysis of dipeptides in the absence of marked changes in enzyme-secreting function of the pancreas. At the same stage, there were changes in motor activity of the stomach with impairment of balance between its two features--amplitude of contractions and rhythm--which ultimately could lead to impairment of processes of evacuation of food (for example, during long-term manned space flights). On the 6th postflight day, we demonstrated a significant increase in activity of enzymes involved in cavitary and parietal hydrolysis of lipids, along with some attenuation of protein hydrolysis, which apparently reflects the need to implement energy processes related to adaptation to earth's gravity. During the long-term readaptation period (30 postflight days), we again found appreciable changes in activity of enzymes involved in parietal hydrolysis of food, namely, depression of protein and carbohydrate hydrolysis with drastic increase in activity of lipolytic enzymes.

Immobilization stress produced in intact animals led to activation of lipase and depression of amylase. We had made analogous findings previously under the effect on intact rats of 2.5 h of immobilization stress [9]. The additional effect of immobilization on animals following the space flight, as well as the set of space flight factors, failed to elicit reactions referable to enzyme-secreting function of the pancreas. The same was observed in a study of pepsin secretion. Use of immobilized stress in intact animals caused an increase in activity of parietal enzymes--monoglyceride lipase and dipeptidase--as well as a decrease in invertase activity. Immobilization of animals following the space flight led to depression of membrane hydrolysis of proteins and carbohydrates, as compared to animals flown in space but not immobilized.

On the whole, it should be noted that the dynamics of changes in most of the parameters studied in animals following a flight in the Cosmos-1129 biosatellite presented the same direction as following the flight aboard the Cosmos-936 biosatellite.

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AMINO ACIDS OF FEMORAL QUADRICEPS OF RATS FOLLOWING FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 24 Jul 81) pp 53-56

[Article by T. F. Vlasova, Ye. B. Miroshnikova, V. V. Polyakov and T. P. Murugova]

> [English abstract from source] The amino acid composition of the quadriceps muscle of rats flown onboard the biosatellite Cosmos-936 and exposed to the ground-based synchronous control experiment was studied. The weightless rats showed changes in the amino acid concentration in the quadriceps muscle. The centrifuged flight and synchronous rats displayed an accumulation of free amino acids in the above muscle.

[Text] Some changes occur in amino acid metabolism of muscle tissue, particularly in the amino acid resources [1-8], under the influence of space flights and conditions that simulate them. We submit here the results of our study of free amino acid levels in the femoral quadriceps of rats following a flight in the Cosmos-936 biosatellite.

Methods

An automatic analyzer was used to assay free amino acids in the rat quadriceps after deproteinization of the samples with sulfosalicylic acid [9, 10]. We used a previously prepared program for analyzing blood plasma specimens [11]. Experimental conditions and designations of groups of animals were described in [12].

Results and Discussion

According to the data in Table 1, the FW_1 [flight, weightlessness] group presented a reliable increase in valine and alanine content 6 h after the flight. There was concurrent decrease in threonine, glycine, serine and aspartic acid. The demonstrated changes in amino acid composition of the muscle affected the overall amount of amino acids, which constituted 99.8% of the level in the VC_1 [vivarium control] group of animals.

Table 1. Free amino acid content of rat quadriceps after flight in Cosmos-936, M/g wet tissue

Amino acid	VC_1, $M \pm m$	C_1^0		FW_1			FC_1			
		$M \pm m$	P_{VC_1}	$M \pm m$	P_{VC_1}	P_{SW_1}	$M \pm m$	P_{VC_1}	$P_{C_1^0}$	P_{SC_1}
Isoleucine	0,23±0,02	0,19±0,01	>0,05	0,23±0,02	0	<0,001	0,35±0,05	>0,1	<0,02	<0,01
Leucine	0,43±0,04	0,33±0,05	>0,1	0,40±0,06	>0,1	<0,001	0,54±0,09	>0,05	>0,05	<0,01
Valine	0,24±0,03	0,21±0,02	>0,1	0,34±0,03	<0,05	<0,01	0,46±0,11	>0,05	<0,05	>0,1
Threonine	2,21±0,27	2,22±0,25	>0,1	1,47±0,14	<0,05	<0,001	2,47±0,16	>0,1	>0,1	>0,1
Serine	0,89±0,05	1,10±0,12	>0,1	0,71±0,04	<0,02	<0,001	1,50±0,15	>0,05	>0,05	>0,1
Methionine	0,17±0,03	0,17±0,02	0	0,22±0,04	>0,1	<0,001	0,27±0,03	<0,02	<0,05	<0,001
Tyrosine	0,20±0,01	0,19±0,04	>0,1	0,16±0,05	>0,1	<0,02	0,26±0,04	>0,1	>0,1	<0,05
Phenylalanine	0,22±0,04	0,16±0,05	>0,1	0,20±0,04	>0,1	<0,01	0,25±0,05	>0,1	>0,1	<0,001
Cystine										
Aspartic acid	0,13±0,03	0,05±0,01	<0,05	0,06±0,01	<0,05	<0,001	0,22±0,06	<0,05	<0,05	>0,1
Glutamic acid	0,83±0,09	1,95±0,37	<0,02	0,94±0,11	>0,1	<0,001	1,80±0,19	>0,1	>0,1	<0,05
Proline	0,53±0,01	0,51±0,02	>0,1	0,67±0,08	>0,1	>0,1	0,50±0,06	>0,1	>0,1	>0,05
Glycine	2,47±0,35	2,53±0,41	>0,1	1,63±0,09	<0,05	<0,001	2,91±0,22	>0,1	>0,1	>0,1
Alanine	2,60±0,16	2,54±0,12	>0,1	3,11±0,15	<0,02	>0,1	3,25±0,17	<0,01	<0,01	>0,1

Table 2. Free amino acid content of rat quadriceps after flight in Cosmos-936, M/g wet tissue

Amino acid	VC_2, $M \pm m$	C_2^0		FW_2			FC_2		
		$M \pm m$	P_{VC_2}	$M \pm m$	P_{VC_2}	P_{SW_2}	$M \pm m$	P_{VC_2}	$P_{C_2^0}$
Isoleucine	0,28±0,06	0,17±0,05	>0,01	0,45±0,07	>0,1	>0,1	0,52±0,11	<0,05	<0,05
Leucine	0,49±0,12	0,29±0,1	>0,1	0,74±0,07	>0,1	>0,1	0,89±0,19	>0,05	>0,05
Valine	0,32±0,05	0,20±0,06	>0,1	0,51±0,06	<0,05	>0,1	0,63±0,09	<0,02	<0,05
Threonine	1,61±0,21	0,93±0,11	<0,05	3,09±0,33	<0,01	>0,05	2,05±0,20	>0,1	<0,002
Serine	1,10±0,11	0,52±0,08	<0,01	1,76±0,21	<0,05	<0,01	1,83±0,05	<0,001	<0,01
Methionine	0,29±0,07	0,18±0,08	>0,1	0,33±0,06	>0,1	<0,05	0,38±0,10	>0,1	>0,1
Tyrosine	0,27±0,07	0,15±0,06	>0,1	0,40±0,07	>0,1	>0,1	0,52±0,12	>0,1	<0,05
Phenylalanine	0,24±0,05	0,16±0,06	>0,1	0,38±0,07	>0,1	>0,1	0,49±0,10	>0,05	<0,05
Cystine									
Aspartic acid	0,23±0,01	0,13±0,04	<0,05	0,31±0,04	>0,05	<0,02	0,47±0,05	<0,002	<0,001
Glutamic acid	0,97±0,14	0,45±0,06	<0,01	2,30±0,17	<0,001	<0,02	1,72±0,21	<0,02	<0,001
Proline	0,53±0,11	0,29±0,04	>0,05	0,89±0,12	>0,05	>0,1	0,70±0,09	>0,1	<0,01
Glycine	2,10±0,18	1,40±0,09	<0,01	3,64±0,25	<0,002	>0,1	3,50±0,27	<0,01	<0,001
Alanine	2,81±0,14	1,31±0,08	<0,001	4,37±0,21	<0,001	>0,1	4,56±0,31	<0,001	<0,001

Table 3. Free amino acid content of rat quadriceps in synchronous experiment, M/g wet tissue

Amino acid	VC_1 $M \pm m$	SW_1		SC_1			VC_3 $M \pm m$	SW_3	
		$M \pm m$	P_{VC_1}	$M \pm m$	P_{VC_1}	$P_{C_1^0}$		$M \pm m$	P_{VC_3}
Isoleucine	0,23±0,02	0,51±0,03	<0,001	0,59±0,03	<0,001	<0,001	0,28±0,06	0,77±0,17	<0,05
Leucine	0,43±0,24	0,79±0,03	<0,001	0,99±0,05	<0,001	<0,001	0,49±0,12	1,59±0,29	<0,01
Valine	0,24±0,03	0,51±0,04	<0,002	0,65±0,04	<0,001	<0,001	0,32±0,05	0,75±0,17	<0,05
Threonine	2,21±0,27	2,33±0,10	>0,1	2,84±0,17	>0,05	>0,05	1,61±0,21	2,13±0,32	>0,05
Serine	0,89±0,05	1,55±0,08	<0,001	1,83±0,30	<0,02	>0,05	1,10±0,11	2,56±0,05	<0,001
Methionine	0,17±0,03	0,30±0,02	<0,02	0,44±0,02	<0,001	<0,001	0,29±0,07	0,86±0,20	<0,05
Tyrosine	0,20±0,01	0,34±0,03	<0,01	0,43±0,04	<0,001	<0,01	0,27±0,07	0,94±0,27	<0,05
Phenylalanine	0,22±0,04	0,39±0,03	<0,01	0,50±0,03	<0,001	<0,001	0,24±0,05	0,83±0,22	<0,05
Cystine									
Aspartic acid	0,13±0,03	0,23±0,02	<0,05	0,34±0,03	<0,001	<0,001	0,23±0,01	0,58±0,06	<0,001
Glutamic acid	0,68±0,09	2,09±0,22	<0,001	2,45±0,17	<0,001	>0,1	0,97±0,14	1,46±0,20	>0,05
Proline	0,53±0,01	0,55±0,08	>0,1	0,70±0,06	<0,05	<0,02	0,53±0,11	0,66±0,06	>0,1
Glycine	2,47±0,35	2,91±0,19	>0,1	2,99±0,26	>0,1	>0,1	2,10±0,18	2,95±0,33	>0,05
Alanine	2,60±0,16	3,36±0,22	<0,05	4,04±0,16	<0,001	<0,001	2,81±0,14	4,12±0,48	<0,05

In the FC_1 [flight, centrifuged] group, there was elevation of isoleucine, valine, aspartic acid and alanine levels in the tested muscle. Overall amino acid content constituted 133 and 122% of the VC_1 and C_1^0 [ground-based centrifuge experiment] controls, respectively. There was an increase in amounts of most amino acids analyzed in the muscle 25 days after the flight in both the FW_3 group (171% of levels in VC_3 group) and FC_2 (162 and 296% of levels in VC_3 and C_2^0 groups, respectively) (Table 2).

Assay of free amino acids in the quadriceps of rats used in the synchronous experiment (SW_1 [synchronous, weightlessness]) 6 h after the experiment revealed a reliable increase in most free amino acids as compared to control levels (VC_1). This elevation affected the total amount of amino acids, which constituted 144% of the levels in the VC_1 group of animals. Amino acid levels remained elevated 25 days after termination of the synchronous experiment (Table 3). In the SC_1 [synchronous experiment, centrifuging] group of animals, there was a reliable increase in amounts of 11 out of the 13 amino acids measured in the quadriceps, and this was reflected in total amino acid content (168% of levels in VC_1 group).

Thus, there was selective increase or decrease in amino acid content of the quadriceps of rats in the FW_1 group as a result of the space flight, the decline being referable to amino acids actively involved in transmination processes and energy metabolism (aspartic acid, glycine, threonine, serine). Conversely, in the FC_1 group of animals, we observed an increase in only a few amino acids (5 out of 13) in the quadriceps, against the background of virtually identical levels in animals of VC_1 and C_1^0 control groups (the only difference was in concentration of aspartic and glutamic acids in the C_1^0 group). There was an increase in free amino acids of animals in the FW_3 and FC_2 groups 25 days after the flight.

The free amino acids levels were above control values for 25 days in the SW_1 and SC_1 groups of animals.

A comparative analysis of our findings revealed that amino acid content of muscle tissue of animals in the FW_1 group selectively increased or decreased, whereas in the FC_1, SW_1 and SC_1 groups of rats it only increased. All of the groups of animals presented an increase in free amino acids 25 days after completion of the experiments.

Analysis of our data revealed that the experimental factors used on animals in the FC_1, SW_1 and SC_1 groups elicited depression of anabolic processes with progressive destruction of protein structures. Ultimately, this led to accumulation of free amino acids in the tissue examined [1, 3, 5, 7, 8]. Weightlessness (FW_1 group) elicited a differentiated change in amino acid content, which is apparently related to a decrease in intensity of protein synthesis [8].

The changes in amino acid metabolism that were demonstrated in the course of this study could be used in the future in developing preventive measures to normalize protein metabolism.

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PLASMA AND TISSUE LIPIDS OF RATS FOLLOWING FLIGHT ABOARD COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 5 Aug 81) pp 56-58

[Article by J. Ahlers, R. A. Tigranyan and M. Praslička (CSSR and USSR)]

[English abstract from source] The content of triglycerides, total phospholipids and nonesterified fatty acids was measured in plasma and tissues of rats flown for 18.5 days on Cosmos-936 in the weightless and centrifuged state. The weightlessness exposure increased lipid fractions in plasma and tissues, and artificial gravity produced a beneficial effect.

[Text] Experiments conducted aboard Cosmos-605, Cosmos-690 and Cosmos-782 biosatellites revealed that prolonged (19.5-22 days) exposure of rats to weightlessness is associated with certain changes in lipid metabolism [1-3]. Our objective here was to determine the effect of artificial gravity [use of centrifuge] on lipid metabolism.

Methods

We conducted these studies on male Wistar-SPF rats (Bratislava, CSSR) flown in space aboard the Cosmos-936 biosatellite for 18.5 days. The experimental conditions and designations of animal groups* were described in [4]. We assayed nonesterified fatty acids (NEFA) [5] in blood plasma, the liver, white (epididymal) and brown (intercapsular) fat, triglycerides (TG) [6] and phospholipids (PL) [7] in plasma, the liver, thymus and bone marrow (humerus), and total cholesterol (C) [8] in plasma and the liver. The findings were processed by the method of variational statistics using the Duncan test [9].

Results and Discussion

Immediately after the flight, there was an increase in blood plasma TG in the FW_1 and FC_1, as well as SW_1 groups of rats; these groups also presented an increase in NEFA concentration. C level was elevated in FC_1 and SW_1 groups of rats, while PL concentration was increased in FW_1 and SW_1 groups. No changes were demonstrable in blood plasma lipids on the 26th postflight day (Table 1).

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*VC--vivarium control; FW--flight, weightlessness; FC--flight, centrifuge; SW--synchronous experiment, weightlessness; SC--synchronous, centrifuge.

Table 1. Composition of blood plasma lipids (M±m)

Animal group	Triglycerides mg%	Total cholesterol, mg%	Phospholipids mg%	NEFA, μeq/ℓ
VC_1	100,8±3,14	63,08±7,09	127,2±8,33	724±55
FW_1	198,2±13,71*	74,36±4,69	175,6±8,57*	1147±114*
FC_1	156,75±4,33*	85,55±5,81*	119,5±8,14	993±97*
SW_1	175,5±4,99*	85,30±4,13*	177,75±3,75*	1337±148
SC_1	116,4±10,2	75,88±6,58	127,00±7,77	716±51
VC_3	113,2±8,59	72,85±1,83	150,75±9,99	712±37
FW_3	105,8±9,16	63,56±1,61	140,60±12,63	823±48
FC_2	95,2±4,89	76,34±2,96	142,60±10,57	754±73
SW_3	82,6±10,4	76,00±3,73	126,20±7,56	461±45

Note: Here and in Tables 2 and 3, mean values for 5-6 animals are given. One and two asterisks refer to values that differ reliably from the vivarium control and corresponding synchronous control group, respectively.

Table 2. Composition of liver lipids (M±m)

Animal group	Triglycerides mg/g	Total cholesterol, mg/g	Phospholipids mg/g	NEFA, μeq/g
VC_1	19,32±1,48	5,16±0,14	31,22±4,64	8,62±0,67
FW_1	29,94±2,80*	6,84±0,34*	26,94±1,34	8,08±0,29
FC_1	21,94±2,81	7,02±0,44*	28,44±1,84	8,94±0,58
SW_1	19,42±2,09	7,52±0,46*	31,22±1,90	10,76±0,32*
SC_1	16,00±2,09	6,58±0,20*	27,30±0,72	9,90±0,43
VC_3	15,10±0,73	5,20±0,18	32,70±0,40	8,96±0,60
FW_3	13,12±2,06	5,06±0,26	35,22±1,20	9,50±0,62
FC_2	16,22±1,44	4,96±0,17	34,86±1,13	10,80±0,93
SW_3	14,76±0,95	5,56±0,11	31,68±1,55	11,24±0,84

Immediately after termination of the experiment, we demonstrated an increase in NEFA concentration in the liver of the SW_1 group of animals and increase in TG content in the FW_1 group. Thus, we failed to demonstrate a correlation between changes in plasma and hepatic NEFA and TG. PL content did not change, whereas C concentration increased in all experimental groups of animals. No changes in composition of liver lipids were demonstrable 26 days after the flight (Table 2).

Immediately after the experiment, there was an increase in concentration of TG in the thymus of FW_1 and FC_1 groups of animals. PL content decreased in all experimental groups. We found an increase in TG concentration in vivarium control rats (VC_3 group) 26 days after completion of the experiment; no changes were demonstrated in FW_3 and SW_3 groups, whereas in the FC_3 group there was a decrease in TG concentration. We failed to demonstrate differences in PL content (Table 3).

There was an increase in concentration of TG in bone marrow immediately after the experiment in all experimental groups of animals; PL content did not change. TG concentration remained high 26 days after the experiment in the FW_3 and SW_3 groups of animals (see Table 3).

Table 3. Lipid composition in the thymus, bone marrow and fatty tissues

Animal group	Thymus		Bone marrow		Fatty tissue	
	triglycer. mg/g	phospholip. mg/g	triglycer. mg/g	phospholip.mg/g	white	brown
					NEFA, μeq/g	
VC$_1$	18,48±1,17	16,10±0,81	45,18±3,98	14,72±1,17	7,17±0,70	6,72±0,46
FW$_1$	43,94±6,55*	13,64±0,35*	101,26±9,15*	12,50±1,56	8,71±0,43	1,84±0,98*,**
FC$_1$	47,85±8,32*,**	14,15±0,28*	55,92±2,40*,**	15,50±1,52	6,66±0,52	15,73±1,39*,**
SW$_1$	23,62±6,03	12,62±0,41*	116,42±16,22*	12,40±1,59	7,14±0,60	10,04±0,53*
SC$_1$	22,12±2,96	12,24±0,92*	88,06±6,45*	12,22±1,61	6,22±0,39	11,24±0,70*
VC$_3$	32,40±4,93*	12,62±0,69	75,10±6,14	15,35±1,76	5,76±0,59	13,78±0,99
FW$_3$	38,24±2,99*	14,18±0,84	134,64±11,35*	15,78±1,44	6,64±0,43	12,46±1,70
FC$_2$	18,38±2,79	12,16±1,23	78,36±5,25	12,40±1,00	6,20±0,24	14,02±1,07
SW$_3$	33,40±2,04*	12,38±0,79	115,04±14,46*	15,72±1,00	6,22±0,73	12,68±0,83

Immediately after termination of the experiment there was a decrease in NEFA concentration in brown fat in the FW$_1$ group of rats, with concurrent increase in FC$_1$, SW$_1$ and SC$_1$ groups of animals. No changes in NEFA content of brown fat were demonstrable on the 26th postflight day. There were no changes in NEFA concentration in white fat of all groups of animals (see Table 3).

Exposure of animals to space flight factors, mainly weightlessness, was instrumental in development of marked changes in lipid composition of tissues and blood. The effect of weightlessness proper was manifested by more distinct changes in flight animals than in those used in the ground-based synchronous experiment. By the end of the readaptation period, all of the altered parameters reverted to base levels. The only exception were the changes in bone marrow.

We should mention the differences between animal reactions to weightlessness and other space flight factors, on the one hand, and reactions to artificial gravity. These differences were more distinct in flight animals than in the synchronous model experiment. Artificial gravity demonstrated a counteraction to weightlessness with regard to bone marrow TG, hepatic TG, plasma PL, as well as (partially) plasma TG. In our opinion, the changes in bone marrow are the most important from the pathogenetic point of view. Accumulation of TG in bone marrow occurred as a result of hypokinesia. We had demonstrated this phenomenon not only during prolonged (46-60 days), but brief (1 day) hypokinesia [10]. Apparently, the decrease in delivery of blood and oxygen transport under hypokinetic conditions, with depression of fatty acid oxidation in cells and stimulation of formation of new cells--adipocytes--is the chief cause of increase in TG content of bone marrow. One should evaluate inhibition of accumulation of TG in bone marrow as the marked beneficial effect of using artificial gravity aboard the biosatellite. The general metabolic changes related to the stress reaction (mobilization of lipids, changes in the thymus) were less responsive to artificial gravity.

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PLASMA AND TISSUE LIPIDS OF RATS FOLLOWING FLIGHT ABOARD THE COSMOS-1129 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 17 Aug 81) pp 58-61

[Article by J. Ahlers, R. A. Tigranyan, I. Djatelinka, B. Schmeida, M. Toropila and M. Praslička (CSSR and USSR)]

> [English abstract from source] Concentrations of triglycerides, total cholesterol, lipid phosphorus and nonesterified fatty acids were measured in blood plasma, liver, thymus, bone marrow and adipose tissues of rats flown for 18.5 days onboard the biosatellite Cosmos-1129. This exposure was accompanied by increases in lipomobilization, content of total cholesterol and lipid phosphorus in plasma, and triglycerides in the thyms and bone marrow. The postflight exposure to repeated stresses demonstrated changes in the lipid content in all animal groups, especially in flight rats.

[Text] The results of previous studies revealed that rats presented changes in composition of lipids of plasma and some tissues [1] immediately after termination of an experiment aboard the Cosmos-782 biosatellite. Use of artificial gravity aboard the Cosmos-936 biosatellite had a beneficial effect on changes in some parameters of lipid metabolism elicited in rats by the set of space flight factors [2].

The purpose of the experiment conducted aboard Cosmos-1129 was to test the effects on animals of recurrent stress in the readaptation period.

Methods

These studies were conducted with male Wistar-SPF rats (Bratislava, CSSR) which were flown in space for 18.5 days aboard the Cosmos-1129 biosatellite. The animals were decapitated 6-8 h after landing and on the 6th postflight day, and some of the animals sacrificed on the 6th postflight day had been submitted to immobilization stress 5 times (for 150 min daily). The rats in the control and synchronous groups were also submitted to repeated immobilization stress.

We assayed nonesterified fatty acids (NEFA) [3] in blood plasma, the liver, white (epididymal) and brown (interscapular) fat, triglycerides (TG) [4] and phospholipids (PL) [5] were assayed in plasma, the liver, thymus and bone marrow, and total cholesterol (C) [6] concentration was determined in plasma and the liver. The obtained results were processed by the method of variation statistics [7].

Results and Discussion

Flight animals presented an increase in plasma C and PL concentration, liver and brown fat NEFA, thymus and particularly bone marrow TG, immediately after landing, as compared to the parameters of vivarium control rats. At this same time, there was an increase (as compared to vivarium control) in plasma C and PL, liver and brown fat NEFA in rats used in the synchronous experiment (Tables 1-3).

Table 1. Lipic concentration in plasma and fatty tissues

Time of examination (number of rats is indicated in parentheses)	Group	Plasma				NEFA	
		TG	C	PL	NEFA,	white	brown
		mM/ℓ			μM/ℓ	μM/g	
After 6-8 h (n = 7)	VC_1	0,78±0,06	1,48±0,11	1,59±0,04	491±68	6,21±1,01	10,7±0,9
	F_1	1,20±0,20	2,25±0,04	2,68±0,10	623±56	5,26±0,99	17,4±1,3
	SE_1	1,26±0,12	2,13±0,21	2,19±0,03	516±86	5,64±0,36	14,8±0,9
After 6 days (n = 6)	VC_2	1,20±0,12	2,30±0,11	1,96±0,16	833±66	5,75±0,31	14,5±0,6
	F_2	0,74±0,07	2,18±0,13	1,75±0,16	697±32	4,77±0,42	16,6±1,1
	SE_2	1,83±0,09	2,21±0,12	1,57±0,11	893±86	4,73±0,29	16,8±1,2
After 6 days + immobilization (n = 7)	VC_3	1,23±0,23	2,09±0,18	1,66±0,11	916±63	7,16±0,77	16,7±0,5
	F_3	1,84±0,20	2,38±0,14	1,84±0,19	1242±114	9,14±0,79	19,6±0,6
	SE_3	0,97±0,10	2,74±0,16	1,77±0,13	903±89	6,16±0,55	16,2±0,8

Key for this and Tables 2-3:

VC) vivarium control   F) flight   SE) synchronous experiment

Table 2. Concentration of lipids in the liver (μM/g)

Time of examination (number of animals given in parentheses)	Group	TG	C	PL	NEFA
After 6-8 g (n = 7)	VC_1	23,6±2,2	13,4±0,50	18,0±1,1	3,69±0,43
	F_1	30,0±2,5	13,2±0,73	17,2±1,1	5,57±0,32
	SE_1	21,9±2,4	11,3±0,28	15,8±0,5	2,52±0,41
After 6 days (n = 6)	VC_2	19,7±2,2	10,2±0,64	16,5±0,7	3,30±0,40
	F_2	22,0±2,0	11,9±0,99	17,6±0,7	5,82±0,39
	SE_2	17,9±1,1	10,9±0,89	16,3±1,1	7,65±0,41
After 6 days + immobilization (n = 7)	VC_3	23,9±2,6	13,3±0,89	17,9±0,6	5,10±0,39
	F_3	31,4±2,7	14,2±1,19	19,0±0,7	8,94±0,40
	SE_3	31,2±2,3	13,9±0,90	16,9±0,6	11,07±0,73

We continued to find an increase in bone marrow TG concentration in flight animals and in liver NEFA in flight and synchronous experiment rats 6 days after the experiment, as compared to parameters of vivarium control animals (see Tables 2 and 3).

As a result of immobilization stress, plasma and bone marrow TG concentration increased, as well as NEFA in plasma, liver and both types of fat in flight rats, as compared to the vivarium control, whereas animals in the synchronous control presented only an increase in plasma C and liver HEFA content (see Tables 1-3).

Table 3. Concentration of lipids (μM/g) in bone marrow and thymus

Time of examination (number of animals given in parentheses)	Group	Bone marrow		Thymus	
		TG	PL	TG	PL
After 6-8 h (n = 7)	VC_1	18,2±6,6	15,4±1,5	17,7±4,7	21,1±0,6
	F_1	51,8±7,0	14,0±0,5	54,0±16,6	23,1±0,9
	SE_1	16,5±5,5	15,3±1,0	26,3±6,3	22,2±0,9
After 6 days (n = 6)	VC_2	13,4±2,5	13,1±2,3	13,2±1,5	19,4±1,0
	F_2	42,4±8,7	10,4±1,1	15,2±1,5	17,3±1,2
	SE_2	34,6±4,5	12,8±1,3	9,7±0,7	17,9±0,7
After 6 days + immobilization (n = 7)	VC_3	29,3±4,9	10,6±1,7	14,2±1,2	21,3±1,8
	F_3	67,1±19,1	10,2±1,0	14,7±1,4	16,6±1,5
	SE_3	23,4±3,7	11,7±0,5	14,1±2,0	18,2±0,7

A comparison of parameters of corresponding animal groups 6 days after landing in order to determine the effect of additional stress revealed that immobilization stress elicited an increase in NEFA content of plasma, the liver and both types of fat, as well as TG in plasma and the liver in flight animals. The animals used in the synchronous experiments presented an increase in C concentration in plasma and the liver, NEFA and TG in the liver, whereas vivarium control rats presented an increase in liver NEFA AND C content, and TG level in bone marrow (see Tables 1-3).

These data indicate that the animals presented virtually the same changes immediately after termination of the Cosmos-1129 experiment as after flight aboard the preceding biosatellite: increased lipid mobilization, increase in levels of some plasma lipids and particularly TG in the thymus and bone marrow [1, 2]; however, there was no accumulation of TG in the liver, which correlated with the increased lipid mobilization in previous experiments. There were less marked changes in rats used in the ground-based synchronous experiment.

We continued to find accumulation of TG in bone marrow 6 days after the biosatellite returned to earth; however, there was disappearance of changes in plasma lipids, signs of lipid mobilization (with the exception of NEFA of liver, which increased) and changes in the thymus. The results of studies pursued after this relatively short postflight period are indicative of rapid repair of some changes in lipid metabolism. It can be assumed that they were caused expressly by the acute stress related to landing of the biosatellite. Conversely, accumulation of TG in bone marrow is, in our opinion, a more specific reaction. From the pathogenetic point of view, it is attributable to weightlessness and hypokinesia, to which the animals were submitted. This reaction also appeared in vivarium control rats after repeated immobilization. The decrease in delivery of blood to bone marrow (concurrently with oxygen deficiency) diminishes oxidation of fatty acids. Some of the findings of morphologists also remind us of de novo adipocyte production in bone marrow of these animals, the general consequence of which is an increase in TG content. Use of artificial gravity aboard the biosatellite inhibits completely the accumulation of TG in bone marrow [2].

Exposure to repeated stress enabled us to demonstrate a number of changes in all groups of animals, particularly the flight groups. Repeated immobilization of rats flown aboard the biosatellite activated entirely mobilization of lipids and accumulation of TG in plasma and the liver, there also being an increase in bone marrow TG content. There were less appreciable changes in rats used in the synchronous experiment and vivarium control; it is particularly difficult to interpret the changes in plasma and liver C content in these groups of animals.

In conclusion, it should be noted that the experiment aboard the Cosmos-1129 biosatellite revealed a number of changes in plasma and tissue lipids, determination thereof by acute stress, on the one hand, weightlessness and hypokinesia, on the other. The less specific changes disappeared rapidly. Repeated stress affected all groups of animals, but the changes were more marked in flight rats.

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MINERAL PHASE AND PROTEIN MATRIX OF RAT OSSEOUS TISSUE FOLLOWING FLIGHT ABOARD THE COSMOS-1129 BIOSATELLITE

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[Article by A. A. Prokhonchukov, K. S. Desyatnichenko, R. A. Tigranyan and N. A. Komissarova]

[English abstract from source] The major parameters of the mineral component and protein matrix of bones were investigated in 30 rats flown onboard Cosmos-1129. Postflight, the content of calcium decreased by 7.8%, that of phosphorus diminished by 11.8%, the Ca/P ratio increased by 5.9%, the content of collagen diminished by 14.7% and that of non-collagenous proteins by 45.7% and the content of sialic and hexuronic acids increased by 36.2% and 14.6%, respectively, as compared to the vivarium control. The paper discusses the role of EDTA-and HCl-protein extracts, soluble and poorly soluble calcium fractions, protein-Ca-phosphate complex, sialic and hexuronic acids in the mechanism of calcium binding by the bone organic matrix.

[Text] The mechanism of mineral loss, mainly Ca^{2+}, by bones is still not entirely clear, in spite of the considerable efforts made to determine this [1, 2]. The experience gained in studying the role of organic matrices in biological decalcification [3-6] shows that disturbances referable to mineral metabolism may be based on changes in organic structures of decalcified tissues.

Organic matrices, which supply nuclei to hydroxyapatite crystals of bone tissue, most of which consists of calcium and phosphorus salts, play an exceptionally important part in providing for dynamic stability of osseous tissue, for its homeostasis. The elements of the organic matrix of osseous tissue, namely collagen and noncollagen proteins, glycoproteins and glycosamine glycans, provide for the bond between organic and mineral phases of bone, mechanisms of fixation and retention of calcium in the skeletal bones [7, 8].

We submit here a comparison of several parameters referable to the state of the organic matrix to levels of macroelements of the mineral phase of bone tissue of rats flown aboard the Cosmos-1129 biosatellite for 19 days.

Methods

We conducted this study on 30 rats divided into the following groups (5 animals in each): rats flown in space and sacrificed immediately after returning to earth (F_1) and 1 month after the flight (F_2), corresponding groups in the ground-based synchronous experiment (S_1 and S_2) and the "pure" vivarium control (V_1 and V_2). We used tissues of the membrane and crest of the scapulae and tibial diaphysis for examination.

Soft tissues were completely removed from bones fixed in ethanol, and they were then ground into powder with a laboratory hard tissue grinder. To assay calcium [9] and phosphorus [10], we submitted 10 mg powder samples to moist ashing by heating it with concentrated hydrochloric acid in Kjeldahl flasks. Collagen and noncollagen protein content was assayed according to Smith [11] after hydrolyzing 50 mg bone power at a temperature of 105-110°C in 6 N HCl for 18 h. To assay polysaccharide components--sialic and uronic acids--we used a modification for mineralized tissues [12] of the methods of Warren and Dische, respectively.

Noncollagen proteins and low molecular peptides of bone were separated by extraction of the bone powder with 0.5 N HCl (100 g tissue in 10 mℓ acid on a magnetic mixer under refrigeration for 18 h), 0.2 N EDTA (under the same conditions) and gel chromatography on 30×1.5 cm columns with G-50 (fine) Sephadex.

Results and Discussion

The changes in amounts of the main constituents of the mineral phase (see Table) did not differ basically from those described previously [13-15], when these elements were assayed in ash of bone samples. Apparently, the most interesting change is the increase in Ca/P ratio in the F_1 group (expressed in gram-atoms--g-atom) indicative of loss of some amorphous calcium phosphate with relative increase in share of hydroxyapatite [16].

There was a 13-15% rise in collagen level of bones in rats sacrificed immediately after the flight (F_1) and synchronous ground-based experiment (S_1). It reverted to virtually the normal value within the readaptation period. The most appreciable change in chemistry of the organic matrix was the 48-42% decrease in noncollagen proteins (according to tyrosine). At the same time, we found a statistically significant increase in amounts of carbohydrate components of noncollagen proteins: by 25% for sialic acids and 14% for hexuronic acids. For this reason, it is logical to assume that the noncollagen protein of bones is represented by several fractions containing different amounts of tyrosine and polysaccharide protein groups.

Analysis of averaged elution profiles of EDTA extracts from the flight group (F_1) and vivarium control (V_1) revealed differences: absence of minor fractions with molecular mass of 20,000-30,000 dalton in the F_1 group and some change in correlation between peaks for the high molecular fraction and peptide fraction (Figure 1). The high molecular protein had a molecular mass of about 60,000 dalton (comparing its yield to that of marker proteins). It contains 4-5 phosphate groups, sialic acids, binds up to 10 atoms of calcium per molecule (according to measurement of activity after incubation with ^{45}Ca).

Mineral and organic components of rat scapula

Animal group	Calcium	Phosphor.	Ca/P, g-atom/g-atom	Collagen	Noncoll protein	Sialic acids	Hexuronic acids
	g/100 g dry defatted bone			g/100 g dry defatted bone		mg/100 g dry defatted bone	
F_1	24,14±0,41	10,80±0,22	1,81±0,02	18,72±0,53	4,75±0,29	114,8±1,5	948,5±13,2
F_2	25,64±0,37	11,94±0,16	1,73±0,01	17,04±0,42	8,64±0,54	94,1±0,9	939,8±27,5
S_1	24,66±0,52	11,08±0,12	1,78±0,01	18,55±0,46	4,78±0,15	108,8±3,9	959,8±59,6
S_2	25,98±0,40	12,30±0,24	1,69±0,02	16,86±0,56	7,78±0,24	91,0±5,6	823,0±21,3
V_1	26,23±0,35	12,24±0,11	1,71±0,01	16,32±0,36	8,75±0,63	84,3±2,3	828,0±16,1
V_2	26,48±0,42	12,32±0,10	1,72±0,01	16,36±0,28	8,64±0,41	86,1±4,0	894,6±22,3

Note: Results differing from corresponding parameters of groups with a significance level of at least 95% according to the U criterion (Wilcoxon-Mann-Whitney) are underlined.

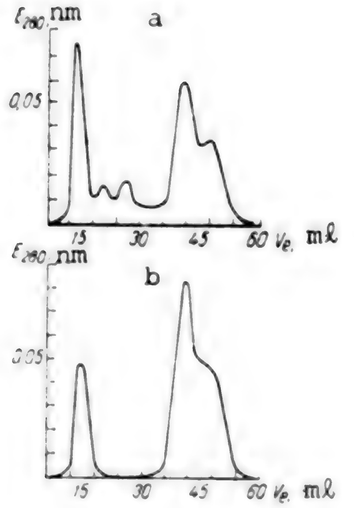

Figure 1.
Chromatographic profiles of EDTA extracts of osseous tissue. Here and in Figure 2:
a) vivarium control (V_1)
b) flight group (F_1)

The elution profiles of the acid extract presented considerably greater differences between the flight (F_1) and vivarium (V_1) groups, which applied both to the values and number of fractions. The fraction contained hydroxyproline, and therefore it was an acid-soluble collagen. Two medium fractions, with yields corresponding to peptide chains with molecular mass of 30,000 to 15,000 dalton, contained hexuronic acids and constituted proteoglycans (Figure 2). For the time being, it is difficult to determine, on the basis of our results, to what is related the increase in their level during the space flight--intensified synthesis or increased extractability due to impairment of intermolecular bonds in the organic matrix of osseous tissue. There was considerable rise of peaks of low molecular peptides, which is perhaps related to proteolytic degradation of the organic matrix. Bone tissue of the F_2 group and synchronous ground-based experiment groups (S_1 and S_2) presented intermediate elution profiles between the flight group (F_1) and vivarium control (V_1).

In order to determine the extent to which disturbances in composition of the organic matrix could cause changes in mineralization of osseous tissue, we conducted an experiment that simulated in vitro partial proteolysis of noncollagen proteins of bones. Samples (of 100 mg powdered intact canine tibia) were suspended in a solution of papain in neutral tris-HCl buffer (1 mg phosphate in 10 mℓ) and buffer without papain (control). After incubation for 24 h at a temperature of 37°C, the bone powder was separated by centrifugation, dried and weighed. We determined the concentration of calcium and phosphorus in the supernatant.

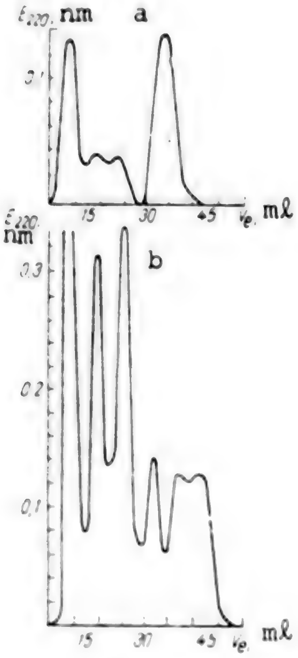

Figure 2.
Chromatographic profiles of HCl extracts of osseous tissue

We found that calcium phosphate is present in supernatant samples (with and without papain) with a Ca/P ratio of about 1.5; however, total inorganic salt content was 3.8 times greater in the samples incubated with papain. During the incubation period the bone samples diminished in mass by 23.1±1.2 mg in solutions containing papain and by 9.7±0.8 mg in solutions without it ($P<0.01$).

Thus, it can be assumed that amorphous calcium phosphate (the most soluble fraction of bone mineral) is bound in a protein-Ca-phosphate complex that is dissociated when the skeleton performs its functions to maintain mineral homeostasis or in the presence of a pathological factor.

The insoluble precipitate present after extraction of bone samples with EDTA and HCl solutions, as well as after papain treatment, contained significant amounts of sialic and hexuronic acids--about half their initial levels. For this reason, it can be assumed that, in addition to fractions of noncollagen protein that effect the bond with the mineral phase, there are others that are more firmly bound with the collagen basis of the matrix, which are probably involved in polymerization of collagen and fibrillogenesis [17].

Thus, we demonstrated complex changes in different directions in amounts of mineral and organic components of osseous tissue after the space flight. On the one hand, we were impressed by the more marked decline of phosphorus level (as compared to calcium) and rise of Ca/P ratio; on the other hand, there were changes in different directions in the protein components: increase (by 14.7%) in collagen proteins and drastic decrease (by 45.7%) in noncollagen proteins of osseous tissue. The presence of unchanging, or more precisely relatively increasing noncollagen protein, along with the collagen fraction, apparently explains the discrepancy in assaying glycoproteins according to tyrosine and carbohydrate components. However, it must be borne in mind that intensification of synthesis of glycosamine glycans and, consequently, the increase in hexuronic acid content could also be related to impaired blood supply to bone tissue [18]. The demonstrated complex changes in mineral and organic component content of osseous tissue confirmed once more the previously found patterns indicative of the leading role of organic components of bone tissue in maintaining dynamic stability (homeostasis) of bones and, in particular, fixation and retention of calcium on skeletal bones with exposure to space flight factors [7, 8].

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NEUROPHYSIOLOGICAL CHARACTERISTICS OF SENSORIMOTOR CORTEX OF RATS SUBMITTED TO EARLY MOTOR DEPRIVATION AND CONDITIONING

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 10 Feb 81) pp 64-70

[Article by I. A. Shimko]

[English abstract from source] Young rats, beginning with the age of 1 month, were kept in small size cages for 3 months, i.e., were exposed to 3-month motor deprivation. This exposure caused a modulating effect of a diminished activity of neuronal populations in the sensorimotor cortex which manifested as a prolongation of the latent periods of primary responses and recovery cycles of excitation of the neuronal populations generating the responses. The differences in the opposite changes in the sensorimotor cortex of the young animals that developed following prolonged deprivation and training of similar duration were seen in the parameters of excitation recovery cycles rather than in the latent periods. The reserve capabilities of the developing cortical structure associated with the modulation of excitation recovery cycles during training were 2.0-2.5 times greater than the dysfunctional changes in the same neuronal populations during motor deprivation. Both early motor deprivation and training did not influence the heterochronic development, emergence and subsequent attainment of the maximum amplitude of components of the testing primary response in the process of a gradual increase of the stimulus-to-stimulus interval.

[Text] Numerous studies established that early individual experience is important to formation of neurophysiological and behavioral reactions of a developing organism [1-6]. When developing animals (cats, rabbits, rats and others) are exposed to heightened sensory stimulation there is improvement of the capacity for forming inborn and conditioned reflex types of behavior, intensification of functional activity of neuronal populations of the cerebral cortex, faster development of synaptic structures of cortical neurons. Keeping animlas in an impoverished environment leads to the opposite effect on functional and morphological development of the central nervous system [7-11].

Figure 1.
Box-cage for individual nonimmobilized animals (motor deprivation of rats); front view

Figure 2.
Locomotor conditioning of rats on treadmill

Data were recently obtained that are indicative of the beneficial role of individual experience in functional recovery of a pathologically developing brain. It was noted that restoration of pathologically altered behavioral and biochemical reactions does not occur spontaneously; rather, it is the consequence of beneficial opportunities provided by an enriched environment in the course of rehabilitating development [12]. Special methods of sensory conditioning may involve affecting the formation of individual brain functions. This has been confirmed by data pertaining to the plastic morphofunctional reorganization of specific populations of cortical neurons in response to visual and sensorimotor stimuli, as well as changes for the better in behavioral acts after surgical injury to the brain of rats and monkeys [4-6, 12].

This aspect of research is quite important, since it offers the possibility of identifying the reserve mechanisms of the developing brain that are involved in adaptation to the environment and compensatory rehabilitation.

Our objective here was to provide the comparative characteristics of functional changes in cortical structures, in particular, the sensorimotor cerebral cortex, according to evoked potentials (EP) of animals submitted to prolonged deprivation and conditioning at an early age.

Methods

These studies were pursued with male Wistar rats divided into two groups, experimental and control (total of 18 animals). The experimental group consisted of 7 animals that were submitted to motor deprivation for 3 months, starting at the age of 1 month, in box cages for individual nonimmobilized animals (Figure 1). The conditions in these cages enabled the rats to perform a limited range of movements and differed from those of "rigid" immobilization hypokinesia. The control group consisted of 11 animals that were kept in large standard cages starting at the age of 1 month, with 4 rats in each cage. Care and feeding of both animal groups were the same.

We tested electrophysiological parameters--EP latency period recorded in the sensorimotor cortex in response to electric stimulation of the peripheral nerve of the foreleg and cycles of restoration of excitability with the use of paired stimuli--after 3 months of motor deprivation. We analyzed changes in excitability on the basis of length of interstimulus intervals (in ms) obtained in the course of gradual increase thereof, with which the amplitude of the negative phase of the primary testing response consistently reached a maximum. The methods used were described in detail in previously published works, in which studies were made of changes in functional activity of the sensorimotor cortex of rats submitted to locomotor conditioning on a treadmill (Figure 2) [6, 13]. These data were used here for comparison of neurophysiological reactions of the brain, which are observed with prolonged locomotor deprivation and conditioning of young animals.

The obtained data were processed by methods of parametric statistics [14].

Results and Discussion

Our results revealed that 3-month motor deprivation of young rats led to 1.7 ms increase in latency periods of primary responses (PR) in the sensorimotor cortex, as estimated from the peak of the positive wave (Figure 3). While average latency periods constituted 13.5±0.44 ms, they were 15.2±0.39 ms in motor-deprived animals (see Figure 3). The statistical reliability of this difference constituted P<0.01. If expressed as a percentage, this change in functional activity of the sensorimotor cortex constituted 12.59±4.41%.

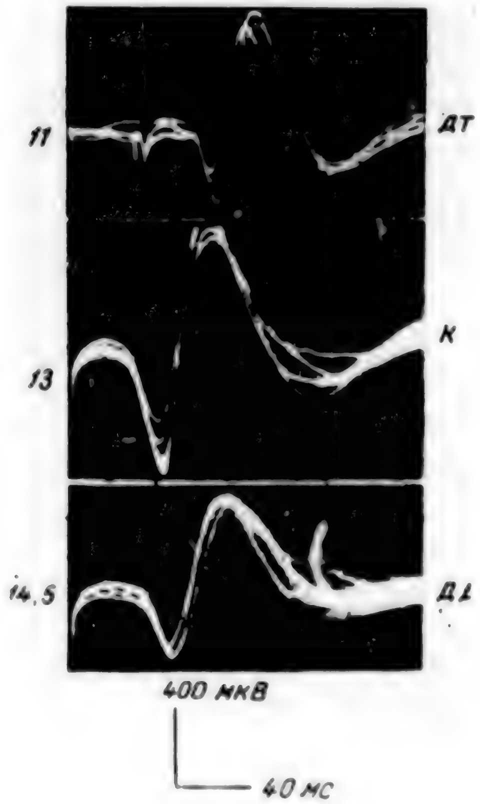

Figure 3.
PR in sensorimotor cortex of rats after motor conditioning (ДТ), motor deprivation (ДД) and in the control (К).

The figures on the left are latency periods according to positive wave peak (ms)

mkB) microvolts
mc) milliseconds

Analysis of cycles of recovery of excitability of neurons of the sensorimotor cortex generating EP in experimental and control rats, as well as following motor conditioning and deprivation, revealed that this EP parameter is highly reactive, as compared to the latency period. In control animals, the cycles of restoration of excitability constituted 97.45±1.78 ms and in experimental animals 103.8±2.37 ms (Figure 4). The increase in cycles of excitability was reliable (P<0.05) in motor deprived animals, as compared to control rats (by 6.35 ms), and constituted 6.52±3.13%. The observed changes in absolute (in milliseconds) cycles of recovery of excitability following motor conditioning and deprivation were indicative of considerably greater functional changes in the case of heightened sensory stimulation. In conditioned animals, the reduction of cycles of recovery of excitability constituted 19.44 ms (P<0.001), which is about 2.5 times more than the increase in the same parameter in deprived animals (6.35 ms; P<0.01). According to relative parameters, the degree of functional changes in populations of sensorimotor cortical neurons in the direction of decrease of this parameter constituted 20.57±3.7% in conditioned animals. At the same time, the increase in cycles of excitability in motor deprived rats constituted, as we have indicated above, only 6.52±3.13% of the base level in the control.

Analysis of PR recorded in the sensorimotor cortex revealed consistent dynamics of changes in configuration of EP in response to the test stimulus with gradual increase in interstimulus interval, not only in control and conditioned rats, but animals submitted to motor deprivation. Thus, with short intervals between stimuli, the response to the testing stimulus was represented by monophasic, superficially positive, low-amplitude waves. Gradual increase in interval between stimuli led to gradual appearance of negative PR to the test stimulus, smooth increase in amplitude of both components of the PR, which subsequently reached and even exceeded the response to a conditioning stimulus. Thus, neither early 3-month motor deprivation nor conditioning contribute any qualitative differences in dynamics of heterochronic appearance of PR components in response to the test stimulus, or changes in maximum amplitude in the course of gradual extension of intervals between stimuli.

These data supplement the results of our prior studies [6, 13, 15], according to which prolonged (3-6 months) locomotor conditioning of rats on a treadmill, begun at the age of 1 month, is associated with statistically significant morphological and functional changes in neuronal populations of the sensorimotor and visual cortex. These changes in the direction of increased functional activity were manifested by reduction of cycles of recovery of excitability in response to paired electric stimulation of the peripheral nerve of the foreleg, as well as reorganization of neuronal dendrites of the fifth layer of the sensorimotor cortex in the form of increase in density of dendritic gemmules. The demonstrated plastic changes in cortical regions of the central nervous system were rather persistent and disappeared only 2 months after discontinuing conditioning.

The results of this study revealed that not only early locomotor conditioning, but deprivation to which rats were submitted at the age of 1 month for a period of 3 months, altered with statistical reliability the functional activity of neuronal populations of the sensorimotor cortex, which was manifested by changes in latency periods of EP and cycles of recovery of excitability. Prolonged restriction of intensity of proprioceptive afferent influx led to plastic changes in neuronal pools of the sensorimotor cortex, but these modifications were in the opposite direction from the functional changes demonstrated in conditioning animals. Diminished reactivity of the sensorimotor cortex in the case of prolonged motor deprivation was manifested by an increase in EP latency periods and cycles of recovery of excitability.

The functional changes demonstrated after motor deprivation, as compared to motor conditioning, were quantitatively manifested the most strongly with reference to the parameters of cycles of restoration of excitability. Thus, while the latency periods changed to about the same degree in deprived and conditioned animals, the severity of changes in cycles of recovery of excitability was 2-2.5 times less after deprivation than after locomotor conditioning. Apparently, the reserve capacities of some functional properties of the nervous system, which were manifested during 3-month conditioning and exceeded the degree of dysfunctional changes in the developing brain after deprivation of the same duration, may have rehabilitation value.

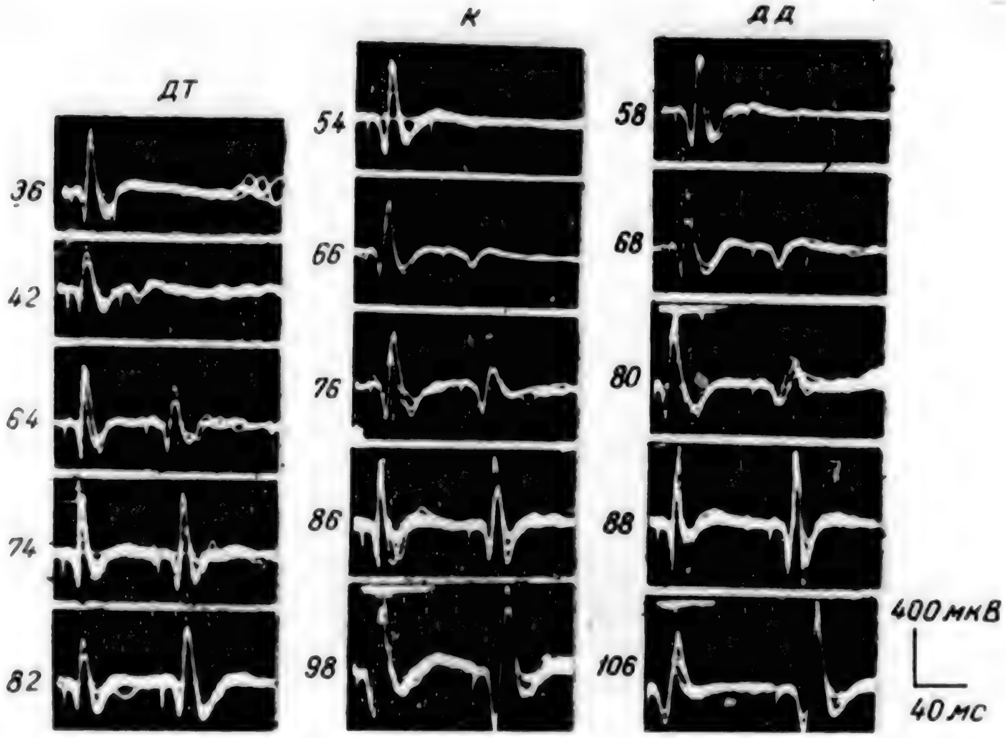

Figure 4. Oscillograms illustrating EP changes in the sensorimotor cortex during the relatively refractory period in response to test stimulus as the interval between it and conditioning stimulus increases, in motor conditioned (ДТ), deprived (ДД) and control (K) rats. The figures on the left show the interval (in ms) between conditioning and testing stimuli.

Key: mkB) microvolts mc) milliseconds

Our data concerning the decline in functional activity of neuronal populations of the sensorimotor cortex with motor deprivation, as well as the thesis that it is possible to make effective use of motor conditioning as a preventive or corrective measure in the case of development of the hypokinetic syndrome, conform with the results of numerous studies in the fields of industrial physiology, sports physiology, space biology and clinical medicine [16-21].

Recently, convincing evidence has been offered of the fact that hypokinetic sickness is associated with development of the asthenization syndrome, which is manifested by physical deconditioning, worsening of work capacity, rapid fatigability, reduction of muscle mass, diminished endurance, development of dyssomnia unstable mood and, in some cases, appearance of mental disorders [18, 22, 23].

Under hypokinetic conditions there is impairment of motor function, locomotor coordination and postural stability, appearance of neurotic disorders, change in immunological reactions and resistance to infection, worsening of blood coagulability and other functions.

Unfortunately, few neurophysiological studies have been pursued under prolonged hypokinetic conditions. The results of existing works deal primarily with analysis of electroencephalographic correlates of the hypokinetic state, and they are indicative of decreased functional activity of the cerebral cortex in the second half of the period of prolonged hypokinesia. This is manifested by a decrease in amplitude of bioelectrical oscillations, change in cortical rhythm in the direction of slow waves, intensification of diffuse, polymorphic slow activity, appearance of waves in the θ and δ ranges, poorer repetition of flickering light rhythm, appearance of paradoxical α rhythm reaction to light, etc. [17, 21, 24-26].

Concurrently, there is change in conditioned reflex and behavioral acts: slower formation of conditioned associations, attenuated orienting reaction, increased latency periods of motor responses, poorer parameters of emotional reactivity, attention, short- and long-term memory [17, 18, 24, 26-28]. As a rule, use of physical exercise during hypokinesia or in the recovery period attenuates or blocks development of dysfunctional changes in the central nervous system or has a beneficial effect on the readaptation period.

At the same time, in spite of the numerous data in the literature that are indicative of the effective preventive and corrective role of motor conditioning in the presence of dysfunctional effects of locomotor deprivation, the question of mechanisms upon which this process is based has been little-studied. Still open is the question of optimum volume of exercise as related to hypokinetic states of different duration, the specifics of conditioning programs, nature and structure of exercises.

At present, we apparently have no solid grounds to interpret the functional changes arising during conditioning and deprivation as two aspects of the same process, since each of them does not always have "mirror" reflections, even with regard to quality of influences, of the specific patterns of enzymatic, structural and neurophysiological reactions [5, 29-31]. In some systems (skeletomuscular system, physiological systems related to physical work capacity, motor coordination) these could indeed be antipodal modifications; in others (neuropsychological functions, immunobiological reactivity, cardiovascular system) there are only partially interacting, overlapping processes. Finally, there are also apparently systems which do not present a pathogenetic link between hypokinetic and postactivation modifications [32].

In view of the foregoing, it may be assumed that prolonged deficiency of proprioceptive afferentation is merely a trigger for the complex pathogenetic mechanism of the hypokinetic syndrome which, in turn, differs basically from the syndrome of poststimulus changes. For this reason, prevention and treatment of hypokinetic disease must not be unilateral. Evidently, they should be based on combined measures, an important element of which must be early motor conditioning.

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HYGIENIC EVALUATION OF NEW TYPES OF RUBBER TO BE USED IN WATER SUPPLY SYSTEMS EXPOSED TO HIGH TEMPERATURES AND ACTIVE CHEMICALS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 13 Apr 81) pp 70-73

[Article by N. I. Omel'yanets, V. I. Lashkareva, N. N. Shabatura and I. S. Kucherov]

[English abstract from source] The paper presents the results of hygienic testing of new rubbers, IRP-2043 and IRP-1136. The rubber IRP-2043 does not change the quality of the water it contacts with. Water extracts of this rubber do not produce a toxic effect on homoiothermal animals. This rubber can therefore be recommended to be used in potable water supply systems. The rubber IRP-1136, when contacting with dechlorinated tap water, alters its organoleptic and physicochemical properties. This rubber cannot be recommended for water supply systems. After a prolonged (18 months) exposure to the condensate of degradation products of the agent 0-30, urine conserving agent and a mixture of urine and the conserving agent the rubbers IRP-2043 and IRP-1136 do not alter physicochemical and bacteriological properties of water or disturb physiological functions of homoiothermal animals. Having this in view, both rubbers can be used in water supply systems functioning at high temperatures and under the influence of active chemicals.

[Text] Work pursued to find various construction materials (metal, rubber, varnish and others) occupies a special place in the problem of studying and developing systems of recovering water from moisture-containing waste. However, the feasibility of using products made of these materials in water supply systems is determined not only by their design, technological and operating properties, but relevant hygienic requirements, since various chemicals that have a deleterious effect on human health may be discharged from the proposed materials into the environment, with which they come in contact.

In the available literature, we found no agreement as to the degree of hazard to human health of rubber, when used to make products and during subsequent operation thereof [1-3]. For this reason, two new brands of rubber, IRP-2046 and IRP-1136, had to be submitted to comprehensive hygienic examination before use in water supply systems.

Our objective here was to determine whether the above brands of rubber could be used in water supply systems exposed to high temperatures and active chemicals.

Methods

IRP-2043 and IRP-1136 rubber was tested in two series of studies. In the first series, we tested the effects of the rubber on properties of distilled water coming in contact with it in 10-ℓ glass aquariums with a 1:1 ratio of surface of rubber to volume of water [4]. An acquarium filled only with distilled water served as a control. In the second series, we tested the effect of active media on the rubber; the composition of the media, as well as model parameters of rubber operation, are listed in the Table. The ratio of tested materials to active media was calculated on the basis of actual conditions of use thereof: 1:5 for condensate from decomposition of product 0-30; 1:10 for rubber:urine preservative; 1:10 for rubber:mixture of urine and preservative.

Composition of working media and model parameters of using IRP-2043 and IRP-1136 types of rubber

Composition of working media	Temperature, °C	Area of rubber in contact with medium, cm^2	Volume of working medium, ℓ
Urine preservative (44.7% concentrated sulfuric acid, 44.3% distilled water, 11% chromium anhydride)	45	100	60
Mixture of urine and preservative (5 mℓ preservative/mℓ urine)	75	400	4500
Condensate from decomposition of product 0-30 (prepared by the following prescription, mg/ℓ: 0.15 samarium, 0.2 tin, 2.5 sodium, 0.2 phsophates, 0.5 hexavalent chromium, 0.5 silver, 0.6 nitrate nitrogen, 0.2 ammonia nitrogen, 0.3 copper, 0.3 hydrogen peroxide; pH 5.0-7.0)	75	400	800

Before immersing the rubber in the tested medium, we submitted it to mechanical washing, first with tap water and soap, then running tap water for 24 h. The water was analyzed immediately, then on the 1st, 2d, 3d, 5th, 7th, 10th, 15th, 20th, 25th and 30th days of contact of the rubber with water and working media, and once a month thereafter to the end of the study period.

Sanitary and chemical testing of water that had been in contact with the rubber samples was performed on the basis of general hygienic and specific parameters, with determination of odor, aftertaste, color, transparency, pH, ammonia nitrogen, nitrates, nitrites, iron, alkalinity, total hardness, permanganate and bichromate oxidizability, unsaturated hydrocarbons and magnesium.

In order to determine whether the rubber could be destroyed by the working media and subsequent passage of decomposition products into water, the tested rubber samples were placed in the above media for long-term (18 months) exposure at temperatures of 45 and 75°C, which was maintained in the drier with fluctuations of ±0.5°C. On the days of the tests, the rubber samples were removed, washed under running tap water, placed in 1 ℓ distilled water, agitated for 1 h, and we then performed a complete chemical analysis of the water, after which the rubber was replaced into the working media.

Survival of saprophytic microflora of river water in the presence of the tested types of rubber served as an indicator of the effects of the rubber samples on bacteria contained in water.

A chronic 6-month sanitary and toxicological experiment was conducted on eight groups of white rats to determine the toxicity of aqueous rubber extracts before and after long-term exposure to the working media. The first group of animals was given aqueous extracts of IRP-2043 in automatic water dispensers, the second group was given water extracts of IRP-1136 rubber, the third IRP-2043 that had been in prolonged contact with a mixture of urine and preservative, the fourth and fifth groups were given the same types of rubber that had been in contact with condensate from decomposition of product 0-30 and urine preservative, respectively; the sixth group was given aqueous extracts of IRP-1136 rubber that had been in contact with urine preservative, the seventh and eighth groups were given rubber of the same type that had been in contact with condensate of decomposition of product 0-30 and a mixture of urine and preservative, respectively. The ninth (control) group was given ordinary dechlorinated tap water. There were 10 animals in each group.

During the toxicological experiment, we monitored the general condition of the animals, their behavior, dynamics of body weight, fluid intake, morphological composition of peripheral blood; we determined activity of cholinesterase and alanine transaminase, assayed urea and total nitrogen of blood serum. We evaluated the functional state of the central nervous system on the basis of behavioral reactions related to investigation of the unconditioning nesting reflex during development of the conditioned motor defense reflex. We also tested the animals resistance to hypoxic hypoxia and changes in bioelectrical activity of the heart submitted to the functional load of hypoxic hypoxia in a pressure chamber. The animals were sacrificed upon terminating the experiment, and their organs were submitted to pathoanatomical and microscopic examination.

The main biochemical and physiological analyses were conducted using previously described techniques [5-7]. The value of the adequate methods we chose is that they permit not only demonstration of any deviations, but classification thereof as compensatory-adaptive, adaptive, insignificant, pathological, etc.

Results and Discussion

The sanitary and chemical studies revealed that IRP-2043 rubber does not alter organoleptic and physicochemical indicators of water quality. During contact with IRP-1136 rubber, we observed appearance of an aftertaste and odor of burned magnesium on the 5th day, the intensity of which reached grades of 4 and 3, respectively, on the 30th day. On the 15th day of contact of the rubber with water, the latter turned light brown. Permanganate and bichromate oxidizability was on the level of 101.3 and 246.8 mg O_2/ℓ, respectively. There was insignificant change in salt composition of water during contact with rubber.

A comparison of the survival rate of saprophytic microflora of river water in the presence of IRP-2043 and IRP-1136 rubber before and after exposing them to the working media for a long period of time revealed that IRP-1136 had a mild inhibitory effect on the 1st and 3d days of the study, and that there was mild stimulation of growth on the 3d day of the tests in a model reservoir of water with IRP-2043 rubber. Throughout the rest of the experiment, the dynamics of development of microflora did not differ from the control.

The toxicological experiment on animals who drank aqueous extracts of IRP-2043 and IRP-1136 water failed to demonstrate changes in their general condition, behavior or dynamics of body weight, as compared to the control group. We also failed to detect appreciable changes in morphology of blood. Our findings revealed that there was a reliable increase in urea content of blood serum in the 2d month of the experiment (to 65.8±3.8 mg% versus 50.2±2.7 mg% in the control; $P<0.01$). Asparagine transaminase activity was also reliably higher in the 1st month (30.0±5.29 versus 16.5±2.12 in the control).

We failed to demonstrate reliable differences in the recorded biochemical parameters of experimental and control groups in subsequent months. Immunological studies failed to demonstrate any influence of aqueous extracts of the tested types of rubber upon the immunological status of the animals. We also found no changes in higher nervous activity of experimental animals. Pathomorphological and histochemical examination of internal organs failed to reveal changes that would be indicative of toxicity of aqueous extracts of IRP-2043 and IRP-1136 rubber. The biochemical changes demonstrated during the first 2 months of the experiment did not exceed the top range of physiological parameters and, since these changes were not observed in subsequent months, they can be evaluated as adaptive.

The objectives of our studies included determination of toxicity of the two types of rubber following prolonged contact with condensate from decomposition of product O-30, urine preservative and a mixture of urine and preservative.

The results of the chronic toxicological experiment we conducted were indicative of transient changes in the animals, the severity of which differed with different working media. Thus, in the 2d month of the experiment on animals given aqueous extracts of IRP-2043 rubber after termination of prolonged contact thereof with a mixture of urine and preservative, there was a rise to 88.0±7.87 mg% in blood serum urea, whereas in animals given aqueous extracts of the same rubber, but after contact with condensate from decomposition of product O-30, it constituted 75.2±8.71 mg% (versus 50.8±2.25 mg% in the control). During the next 4 months of the experiments, we failed to demonstrate appreciable differences in biochemical parameters and immunological system of blood between the control and experimental groups of animals. The statistically reliable differences we noted in morphological composition of blood were within the normal range for this animal species. None of the groups of animals given aqueous extracts of IRP-2043 rubber after contact with working media presented changes in higher nervous activity, nor were there any reliable differences in any of the recorded parameters of bioelectrical activity of the heart.

Observation of animals given aqueous extracts of IRP-1136 rubber after long-term contact with condensate of decomposition products of agent 0-30, urine preservative and mixture of urine and preservative failed to demonstrate differences in behavior, general condition and dynamics of body weight, as compared to control animals. We also failed to note changes in morphology and immunological system of blood; there were no changes in animal resistance to hypoxia.

Insignificant changes in higher nervous activity were demonstrated in animals given aqueous extracts of IRP-1136 rubber that had been in contact with the condensate from decomposition of agent 0-30 and a mixture of urine and preservative: orienting behavior and nesting reflex were well-marked by the end of the 3d experimental month; the elementary defense reflex in response to the situation was developed in 85.7%, which differs negligibly from the control (92.7%).

These studies revealed that IRP-2043 rubber does not alter organoleptic and physicochemical properties of water; aqueous extracts of this rubber had no toxic effect on homoiothermic animals. Organic compounds pass from IRP-1136 rubber into the water, with which it comes in contact. This serves as grounds to recommend only IRP-2043 rubber for use in potable water supply systems.

After discontinuing exposure of IRP-2043 and IRP-1136 to condensate from decomposition products of agent 0-30, urine preservative and mixture of urine and preservative for a long time (18 months), there was virtually no change in physicochemical and bacteriological parameters of water quality; there was no appreciable functional impairment of organs and systems of warm-blooded animals. This enables us to recommend both types of rubber for water supply systems exposed to high temperatures and active chemicals.

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AEROSOL POLLUTION OF AIRTIGHT HABITATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 21 May 81) pp 73-76

[Article by B. V. Anisimov, T. I. Golubeva, G. N. Kuz'menko and V. P. Savina]

[English abstract from source] The paper discusses the man's contribution to the formation of aerosol particles in manned enclosures. The data obtained in prolonged simulation studies suggest that man is the major source of aerosol contamination. The aerosol concentration and disperse composition are found to depend on the free volume per man. The paper presents for the first time the data on the rate of dust formation in manned enclosures.

[Text] Accumulation of aerosol in the gas atmosphere of manned spacecraft cabins could lead to considerable worsening of the cosmonauts' living conditions. There have been indications in the literature of the need to detect the sources of aerosol pollution of cabins even before long-term space flights were made [1]. To date, only the results of studying bacterial aerosol have been published [2, 3]. Particles carrying bacteria constitute an insignificant share of aerosol particles, so that microbiological studies cannot assess aerosol pollution of the gas atmosphere of confined habitats.

According to data in the literature, man is one of the sources of aerosol particles in confined habitats. A clothed man emits 10^5 to $3 \cdot 10^7$ particles/min (depending on his physical activity). The intensity of emitting particles bearing bacteria is lower by several orders of magnitude and constitutes several tens [2, 3] to 10^3/min [4].

We conducted this study in order to obtain quantitative and qualitative characteristics of aerosol in pressurized habitats.

Methods

Studies were conducted in two pressurized compartments 24 and 140 m^3 in size. In the studies with the small chamber, the free volume per subject was changed by placing airtight containers or changing the number of subjects used in the test. We ran 6 tests in the small chamber lasting 15 to 40 days and one in the large chamber lasting 90 days. In all of the studies, we maintained a normal microclimate by means of a system of recycling and conditioning the gas atmosphere. The subjects wore woolen exercise suits, cotton underwear and sports shoes.

Table 1. Estimated concentration of aerosol particles over 0.4 μm in diameter

Parameter	Number of subjects in chamber				
	4	2	2	1	3
Free volume, m^3/person	6	8	12	24	46
Particle concentration, $\times 10^3/\ell$	38±6 (12—55)	17±3 (8—32)	14±3 (5—22)	6,5±1,3 (3—17)	2,5±0,6 (1,4—6)
Number of readings	59	16	10	10	36
Quantity of particles in free volume per person	$2{,}3\cdot 10^8$	$1{,}3\cdot 10^8$	$1{,}7\cdot 10^8$	$1{,}6\cdot 10^8$	$1{,}15\cdot 10^8$

Note: Extreme values are given in parentheses.

The estimated concentration and distribution of particles according to size (from 0.4 to 10 μm in diameter) were determined with an AZ-5 photoelectric counter; weight concentration was determined by the standard method, collecting aerosol on AFA-VP-20 filters. During the tests in the 140-m^3 chamber, it was possible to collect settled dust and refuse regularly with a vacuum cleaner. To identify the aerosol particles, we examined the sediment collected on transparent "Nuklepor" filters under a microscope. The dust picked up with the vacuum cleaner was also examined under a microscope. We used conventional methods [5] to determine the distribution of aerosol particles according to size. We used the nonparametric criterion of Wilcoxson-Mann-Whitney to determine differences in estimated concentration of aerosol. The results of measuring the concentration of aerosol by weight were compared by the method of Student.

Results and Discussion

In the background studies (without man) the calculated concentration of aerosol slowly diminished. The gas atmosphere was purified both with and without air conditioning system operation. There was a 2-9-fold decrease in number of particles with more than 0.4 μm diameter, 10-25-fold decrease in those with more than 1 μm diameter, while particles with a diameter of 4 μm were usually not demonstrable over a 24-h period with the air conditioning system turned on. The weight concentration could not be measured in the background studies, since more than 24 h were required to collected a batch of 1 mg on the filter, as required by the method. According to a tentative estimate, the concentration of aerosol was less than 0.005 mg/m^3 after 24 h in the pressure chambers, in the background studies.

In the manned pressure chambers, the estimated aerosol concentration fluctuated over a wide range. There usually were 2-3-fold changes in concentration over a 24-h period. We were unable to determine the entire causes of these fluctuations. The decrease in particle concentration during the periods of daytime naps and at night were obviously related to the decreased activity of subjects in the pressure chamber. There was an increase in concentration of large particles (2-10 μm) when changing bed linens and an increase in fine particles (0.4-0.7 μm) when preparing food.

Table 2. Weight concentration of aerosol

Parameter	Free volume/person, m^3			
	6	12	24	46
Aerosol concentration, mg/m^3	0,14±0,002	0,10±0,007	0,06±0,01	0,02±0,005
Aerosol content, mg/person	0,84	1,2	1,44	0,92

Table 3. Amount of dust collected with vacuum cleaner in $140\text{-}m^3$ chamber

Measurement No	Duration of dust collection, days	Dust weight, g	Amount of dust, g/man/day
1	40	78.3	0.65
2	7	50.3	2.4
3	7	83.5	3.9
4	10	61.7	2.1

A comparison of the results of different studies (Tables 1 and 2) revealed that estimated and weight concentrations of aerosol increase with reduction of free volume per person. The differences between the different studies (see Tables 1 and 2) are statistically reliable. Our findings are consistent with the data in the monograph of G. I. Karpukhin [6] concerning the dependence of levels of bacterial aerosol in manned habitats on population density and activity of people. The obtained data confirm information in the literature to the effect that man is the main source of aerosol in pressurized rooms. The amount of aerosol in the free volume per man was of the same order of magnitude in all of the studies. This warrants the assumption that the intensity of formation of aerosol particles by subjects fluctuated over a narrow range in all of the tests.

According to the results listed in Table 3, the amount of dust formed in the course of man's routine activities constitutes several grams per man per day. The figures listed in Table 3 are apparently low estimates of intensity of dust formation, since only part of the dust could be picked up with the vacuum cleaner.

Microscopic examination of filters revealed fibers from clothing, bed linen, particles of epidermis and a small amount of mineral particles. The dust picked up by the vacuum cleaner consisted of the usual household refuse:

food crumbs, hair, clothing fibers and a significant part consisted of agglomerates of fine particles.

Table 4. Sizes of aerosol particles in pressurized chambers as a function of specific volume

Particle diameter µm	Share of particles, %		
	free volume per person, m^3		
	46	12	6
0,5	34±1,6	45±2	60±3,2
0,6	[illegible]±3,0	19±1,5	39±3,2
0,7	16±2,1	12±1,3	3[illegible]±3,3
0,8	9±0,8	7,6±1,1	24±3,0
0,9	4±0,3	5,5±1,1	21±3,1
1,0	2,5±0,6	3,6±0,8	15,3±2,6
1,5	1,8±0,3	2,6±0,2	11±2,2
2,0	0,9±0,2	1,6±0,5	8,8±1,6
4,0	0,3±0,15	0,6±0,2	2,8±0,5
7,0	0,15±0,04	0,2±0,04	1,1±0,2
10	0,04±0,015	0,08±0,01	0,3±0,05

Note: The concentration of particles with a diameter in excess of 0.4 µm was taken as 100%.

As can be seen in Table 4, with reduction of free volume per person, the size of aerosol particles changed in the direction of an increase in share of large ones. Hence, it can be concluded that anthropogenic aerosol is characterized by large particles. In weightlessness, there will probably be production of anthropogenic particles 0.4-10 µm in size at the same rate as on earth. There would not be significant pollution of the cabin's gas atmosphere by this size of anthropogenic particles. Large particles, (over 20-30 µm), which settle rapidly at the usual gravity, will constitute most of the aerosol in weightlessness. The quantity of such large particles of anthropogenic origin in the gas atmosphere of an orbital station could exceed significantly the hygienic standards during a long-term flight. There is some probability of mechanical injury to the upper respiratory tract and allergic disease when there is a high concentration of large particles [7]. For this reason, it is a pressing task, in our opinion, to develop research and measures for the prevention of pollution of the gas atmosphere of spacecraft by anthropogenic aerosol.

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MAN'S ADAPTIVE REACTIONS TO ACOUSTIC PARAMETERS OF ISOLATED HABITATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 13 Feb 81) pp 76-81

[Article by G. A. Manovtsev, V. A. Korsakov, G. I. Odinokov and V. A. Stepanov]

[English abstract from source] The study of acceptability of noise levels, subjective evaluation of the acoustic environment by the test subjects, and examination of their cardiovascular function demonstrated the development of adaptive reactions to the noise effects which were accompanied by a certain tension in the cardiovascular system.

[Text] Noise plays an important part in the set of factors that characterize man's distinctive living conditions in pressurized chambers. Under such conditions, the acoustic environment is formed as the result of operation of different elements of life support systems, units, equipment and communication devices. The specific feature of noise, to which man is exposed in an isolated space, is its constant presence since the need to maintain specified parameters of the habitat requires virtually continuous operation of life support systems. Another distinction of the acoustic environment in an isolated compartment could be the lack of considerable sonic pressure gradients in work and rest places. There have been a number of studies of the effects on man of the acoustic factor in pressurized spaces and with exposure to various conditions inherent in space flights [1-6].

The results of experimental and clinical studies indicate that intensive noise has the most deleterious effect on the auditory analyzer [7, 8]. L. A. Orbeli indicated that the reaction of the auditory analyzer to loud sounds depends not only on the force of the sound, but excitability of the central nervous system which, in turn, alters excitability and lability of the auditory analyzer [9]. The influence of noise is not limited to its specific effect on this analyzer, and it could lead to nonspecific reactions of the integral organism, which are manifested in the form of diverse functional changes associated chiefly with impairment of the autonomic nervous system. During exposure to noise, according ot the data of most authors, the functional change in the autonomic nervous system precedes direct impairment of auditory sensitivity [10-13].

Studies have shown that there are marked autonomic reactions associated with changes in cardiac function, circulation in different organs and arterial pressure with exposure to intensive noise [14]. The hemodynamic disturbances in individuals exposed to noise may be generalized, often in different directions with prevalence of hypertensive states, and they are attributable to impaired neuroreflex regulation of the circulatory system [15].

When there are a set of factors involved, the effect of noise on man may be enhanced by the effects of altered living conditions. At the present time, we have information to the effect that the effect of noise on man is intensified under adverse microclimate conditions [16]. Simulation of noise factors is of special importance in determining the significance of the acoustic factor when man is exposed to a set of deleterious factors [12].

We submit here an evaluation of the effects on man of the acoustic parameters of his environment in the case of concurrent presence of the set of factors inherent in a pressurized space. Numerous stuides [6, 12, 17, 18] have shown that prolonged exposure to noise first causes changes in the central nervous and cardiovascular systems, and only then reduces auditory sensitivity. In this experiment, we limited ourselves to investigation of the cardiovascular system to assess man's reactions to noise. In order to demonstrate physiological reactions directly attributable to the effect of noise, we used a functional test with simulation of the noise inherent in the period of operator work by the participants in the experiment. The methodological approach we used enabled us to assume that there is a correlation between the effect of noise and dynamics of cardiac function during the functional test.

Methods

Three volunteer subjects spent 25 days in an isolated [airtight] chamber, the compartments of which were functionally separated into work zones and rest zones. We used a mixed (according to sleep time) schedule of work and rest, consisting of 12-h work (operator work during duty period ["watch"]), 12-h subduty period (brief replacement during work shift of main operator) and 12-h rest period. Various units of the life support system were the main sources of noise. Sonic pressure was measured at the work places and rest zones with a GDR-made sound meter [noise gauge].

In order to evaluate the changes due to noise, the subjects made a subjective assessment of the acoustic situation, acceptability of noise level on the basis of analysis of daily dynamics of movements of the subjects in the compartments of the chamber and we recorded the dynamics of cardiac function. The questionnaire method was used for subjective evaluation of noise, with analysis of changes in perception throughout the experiment. To determine the acceptability of noise levels, we conducted concealed observation and recorded the movements of the subjects directly caused by noise. We took into consideration the complaints about the noise, requests to turn off different sources of noise, frequency of using individual fans in the cabins during rest, subjects' choice of a place, as related to location of the noise source, etc.

We used the polycardiographic method of examining the phase structure of the left ventricular systole according to Blamberger, as modified by V. L. Karpman

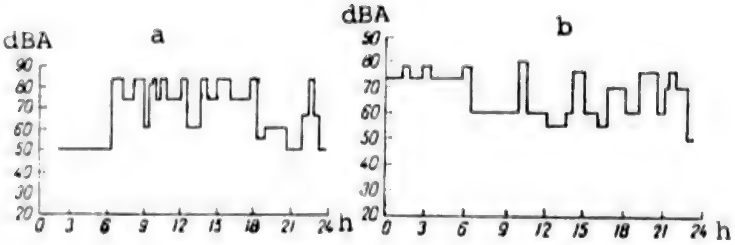
[19] to record dynamics of cardiac function. We took these tracings in the rest zone with the subjects supine in the presence of an acoustic background in the first and 5th minutes of simulating the noise in the work zone of the instrument compartment--IC (sonic pressure constituted 84 dB in the region of the subject's head) and in the 3d min of the noise aftereffect period. Automatic processing and isolation of different time intervals of the cardiac cycle were performed on a real time scale using a computer complex, which included a special analyzer of polycardiographic signals, digital converter and calculator with digital printer. The processing program included calculation of nominal values of phases and periods of the cardiac cycle [20]. The Student criterion was used for statistical processing of the results of the studies.

Results and Discussion

Table 1 lists the levels of sonic pressure in the sealed chamber in the zone of operating equipment (IC) and spectral characteristics of the different sound sources. According to the submitted data, there is wide-band noise in the chamber, with some elevation of sonic pressure in the region of 1000, 2000 and 4000 Hz. On the basis of analysis of time spent by the subjects in different compartments of the chamber, related mainly to the specified work and rest schedule, we plotted the average 24-h curves of noise levels for duty and subduty periods (see Figure). On the whole, the noise level changed in the range of 47-85 dBA throughout the study. During the work period, noise was in the range of 60-85 dBA and during the rest priod 47-60 dBA. The acoustic situation was markedly dynamic and was rather completely determined by the daily schedule. Standing waves were established in the acoustic field of the work compartment, with fluctuations of sonic pressure in the range of 8-12 dB.

Table 1. Levels of sonic pressure and spectral characteristics of main sources of noise

Noise source and operating mode	Place of measurement	Sonic pressure, dB	Sound level dBA	Sonic pressure (dB) at geometric mean frequencies, Hz							
				63	125	250	500	1000	2000	4000	8000
Acoustic background	Cabin	48	30	44	34	30	25	20	20	15	15
Unit 1	IC, near system	74	73	44	50	58	52	62	72	65	56
Unit 2	Same	81	80	60	58	62	63	74	79	79	64
Unit 1	IC, between systems	79	78	44	48	62	56	68	76	72	58
Unit 2	Same	88	84	64	64	65	65	76	84	80	70
Unit 3	IC, near system	67	66	56	59	56	62	61	52	48	46
Unit 3	IC, between systems	73	73	45	52	60	71	67	60	58	52
Fan 1, minimum speed	Cabin 1	55	47	45	38	40	41	42	40	35	25
Fan 1, maximum speed	Same	56	50	49	40	39	47	44	43	35	25
Fan 2	IC, main console	68	66	58	40	46	50	64	60	52	42



Averaged daily curves
of noise levels
a) duty period
b) subduty period

During the study, the subjects assessed the effect of noise as "insignificant," and by the end of this period there was an increase in opinions that "the noise is no bother." This is indicative of some habituation to the noise. Analysis of movements of subjects related to the acoustic situation in the chamber led us to conclude that the permissible noise level during work was in the range of 70-80 dBA. In the rest period it dropped from 65-70 to 50 dBA and stabilized at this level toward the end of the experiment. The relatively high level of subjectively permissible noise during the work period is apparently attributable to the distinctions of the acoustic situation in the pressurized compartment, which provided for rest at a noise level 20-30 dB lower than the noise during the work period.

The microclimate parameters and gas atmosphere in the chamber were close to optimum (CO_2 concentration 0.5-0.8%, relative humidity 40-70%, atmospheric temperature 20-23°C) during the 1st-13th and 22d-25th days. The microclimate and gas composition were altered (CO_2 concentration 1.8-2.7%, relative humidity 50-90%, atmospheric temperature 25-32°C) between the 14th and 21st days.

During the background studies prior to sealing the chamber, the functional test with simulation of effects of noise was associated with alteration of phase structure of the cardiac cycle with changes in the same direction in some phases and systolic periods of the left ventricle (Table 2). In the 5th min of exposure to noise, all of the subjects presented an increase in duration of the phase of asynchronous contraction, reduction of period of isometric contraction, reduction of expulsion, mechanical and total systole. There were statistically reliable changes in all subjects in phases of asynchronous contraction and mechanical systole, but the values did not exceed the physiological range. In 2 subjects, the duration of the cardiac cycle and diastolic period diminished (reliable changes) and the intrasystolic index was slightly elevated by the 5th min of exposure to noise. In accordance with the classification of V. L. Karpman [19], the decrease in duration of isometric contraction phase, expulsion period, mechanical systole and elevation of intrasystolic index correspond to the phase syndrome of myocardial hyperdynamia which is inherent in muscular work, emotional stress states, etc., under physiological conditions. In the author's opinion, the phase changes are not related to extracardiac influences, since they are demonstrable at the very start of physiological perturbances in the absence of changes in venous return and with normal diastolic pressure.

Table 2. Direction of changes in phase structure of left ventricular systole under the influence of noise

Physiological parameter	Before the study				24th day of study			
	$M_1 \pm m$	$M_2 \pm m$	$M_2 - M_1$	P	$M_1 \pm m$	$M_2 \pm m$	$M_2 - M_1$	P
Subject K.								
Duration of cardiac cycle	1072±9	944±6	−128	<0,001	1104±3	1093±11	−11	
Diastole	675±7	552±5	−123	<0,001	704±4	700±12	−4	
Electric systole	399±2	391±4	−8		374±1	375±1	+1	
Asynchronous contraction	66±1	71±1	+5	<0,01	70±1	71±2	+1	
Isometric contraction	53±3	46±2	−7		45±4	36±2	−9	
Tension [contraction] period	119±3	118±1	−1		115±4	107±3	−8	
Ejection period	278±2	274±1	−4		284±3	287±2	+3	
Mechanical systole	331±3	320±2	−11	<0,05	329±2	323±2	−6	<0,05
Total systole	397±3	392±1	−5		399±2	394±3	−5	
Protodiastole	32±1	35±1	+3	<0,01	37±2	30±1	−7	<0,01
Intrasystolic index	84±1	86±0,4	+2		86±1	89±1	+3	
Subject T.								
Duration of cardiac cycle	974±7	921±18	−53	<0,05	979±6	987±10	+8	
Diastole	623±5	577±17	−46	<0,05	605±5	607±9	+2	
Electric systole	358±2	351±3	−7		358±2	361±2	+3	
Asynchronous contraction	44±1	57±3	+13	<0,01	48±2	57±2	+9	<0,05
Isometric contraction	49±3	33±3	−16	<0,01	44±2	46±4	+2	
Tension period	92±3	90±3	−2		92±2	103±2	+11	<0,01
Ejection period	258±2	253±4	−5		282±1	277±2	−5	<0,05
Mechanical systole	307±4	286±3	−21	<0,001	327±2	323±3	−4	
Total systole	351±3	343±2	−8		374±2	380±1	−6	
Protodiastole	34±1	34±1	0		26±1	28±1	+2	
Intrasystolic index	84±1	89±1	+5	<0,01	86±1	86±1	0	
Subject F.								
Duration of cardiac cycle	971±3	978±9	+7		1185±16	1163±13	−22	
Diastole	606±4	612±9	+6		784±15	768±14	−16	
Electric systole	357±2	357±1	0		372±2	377±1	+5	
Asynchronous contraction	56±3	71±2	+15	<0,001	67±1	68±1	+1	
Isometric contraction	13±2	11±3	−2		29±2	26±3	−3	
Tension period	70±1	82±2	+12	<0,001	96±2	91±5	−5	
Ejection period	296±3	281±2	−15	<0,01	306±2	304±1	−2	
Mechanical systole	309±4	292±2	−17	<0,01	335±2	360±13	+25	
Total systole	366±3	366±4	+07		401±2	395±5	−6	
Protodiastole	25±1	38±1	+8	<0,001	29±0,4	37±1	+8	<0,001
Intrasystolic index	96±1	96±1	0		91±0,4	85±3	−6	

Note: M_1±m--mean parameter and mean error before noise; M_2±m--mean parameter and mean error in 5th min of noise; phases and periods of systole are given in milliseconds, intrasystolic index is given as a percentage.

On the 24th day of isolation of subjects in the chamber, 5-min simulation of sound was not associated with marked and unidirectional changes in phase structure of the left ventricular systole. We observed negligible increase in electric systole and phase of asynchronous contraction. This reaction warrants the belief that the subjects developed adaptive changes in response to the acoustic situation in the chamber, as a result of which there was no unidirectional alteration of phase structure during exposure to the functional noise test by the end of the experimental period. The changes in structure of the cardiac cycle in the first minute of simulation of noise were analogous in direction to those observed in the 5th min of noise, but they were less marked.

According to V. L. Karpman [19], the duration of the phase of asynchronous contraction is determined primarily by the state of metabolism in the myocardium, which regulates the rate of propagation of depolarization and electromechanical latency period in each contractile element. In the opinion of Holldack [21], the duration of asynchronous contraction depends on filling pressure. Numerous studies [15, 22] established that noise affects the central and autonomic nervous systems, first of all, as well as reticular formation of the brain, eliciting intensive cardiovascular reactions. This circumstance and the distinctive change in phase structure in the presence of noise prior to the study (reliable changes in phase of asynchronous contraction) warrant the belief that the reactions are of an emotional stress nature, with alteration of dynamics of the cardiac cycle as a result of extracardiac regulatory influences.

As compared to the period prior to the experiment, during the subjects' stay in the isolation chamber there was an increase in virtually all systolic intervals of the left ventricle. All of the subjects presented a statistically reliable increase in ejection period ($P<0.001$) and duration of cardiac cycle ($P<0.05$). There were analogous changes demonstrated in previous studies involving prolonged isolation of man in a pressure chamber [23]. The distinctive finding of our studies was a reduction in duration of ejection period, as compared to nominal values, which is indicative of some strain on the circulatory system.

The results of testing the permissibility of noise levels used, subjective assessment of the acoustic situation by the subjects and analysis of dynamics of cardiac function are indicative of development of adaptive changes in response to noise, which take place against a background of some strain on the circulatory system. A relatively high noise level during the work period (up to 85 dBA) did not elicit marked reactions, and this is apparently attributable to the specifics of noise modes used, with which the subjects were allowed to rest at a noise level that was 20-30 dBA lower than during the work period.

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AGE-RELATED DISTINCTIONS OF ECHOCARDIOGRAPHIC PARAMETERS OF HEALTHY MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 15 Apr 81) pp 82-84

[Article by A. M. Babin]

[English abstract from source] Certain parameters of intracardiac hemodynamics and myocardial contractility of healthy men were examined by echocardiography. Age-related variations of these parameters were seen in representatives of different age groups. The paper emphasizes that echocardiography may find a wider application in space medicine.

[Text] We know that space flights can lead to changes in activity of the human cardiovascular system [1-4]. For this reason, special investigations of the nature and mechanisms of development of functional disturbances in the heart during and after flights, as well as with simulation of some of the effects of weightlessness on the ground, acquired special importance in recent years. The cardiological examination of cosmonauts can be substantially improved by using new ultrasonic diagnostic methods, in particular, echocardiography. At the present time, a few reports have already been published on the use of echocardiography as a method of examining the heart in model experiments [5-7], as well as for examination of spacecraft crews [9, 10].

However, since echocardiography had been used in clinical practice only for diagnostic purposes until recently, the publications were concerned primarily with cardiac pathology. For this reason, the question of echocardiographic parameters of the heart of healthy people in different age groups is still open.

Since we presently observe a tendency toward increase in the age of cosmonauts, it is quite important to have information about the condition of the cardiovascular system in individuals of older age groups.

We studied here the functional state of the cardiovascular system by means of echocardiography in resting individuals of different age groups, with determination of standard echocardiographic parameters and their age-related dynamics.

Echocardiographic parameters of healthy subjects in different age groups (M±m)

Parameter	Group					Mean values
	1	2	3	4	5	
Ds	3,09±0.04	3,21±0,04	3,40**±0,07	3,60*±0,10	3,70*±0,09	3,40±0,04
Dd	5,04±0,11	5,20*±0.05	5,20*±0,08	5,40*±0.07	5,70*±±0,08****	5,30±0,04
ESV	37,60±1,11	44,10*±1,51	46,30*±2,21	55,50*±3,71***	60,10*±3,43	48,10±1,10
EDV	120,70±5,63	127,03±2,57	130,60±4,04	140,40*±4,06***	156,96*±5,78****	134,60±1,64
SV	83,20±5,39	85,40±1,61	84,30±4,07	84,90±4,91	96,90*±4,22	86,90±0,68
OF	68,40±1,43	67,30±0,65	64,50±1,77	60,10*±2,79	55,60*±2,50	63,20±0,56
SF	38,70±1,21	37,90±0,50	35,60±1,36	34,40±2,11	34,0±0,39	36,10±0,30
RCR	1,38±0,05	1,32±0,03	1,23*±0,04	1,13*±0,06	1,09*±0,05	1,23±0,02
CRpw	4,47±0,19	4,56±0,14	4,43±0,09	4,43±0,09	4,33±0,14	4,44±0,01
RRpw	10,63±0,28	10,12±0,50	9,49*±0,18	9,14*±0,57	7,56*±0,31****	9,39±0,18
CRs	2,98±0,14	2,87±0,13	3,03±0,20	3,74±0,53	3,29±0,25	3,18±0,04
RRs	2,58±0,10	3,04±0,15	3,30*±0,18	4,32*±0,56***	3,07*±0,27****	3,26±0,08

Note: One asterisk refers to reliable difference from 1st group of subjects; two, three and four asterisks refer to reliable difference between parameters of 2d and 3d, 3d and 4th, 4th and 5th groups, respectively (with $P<0.05$).

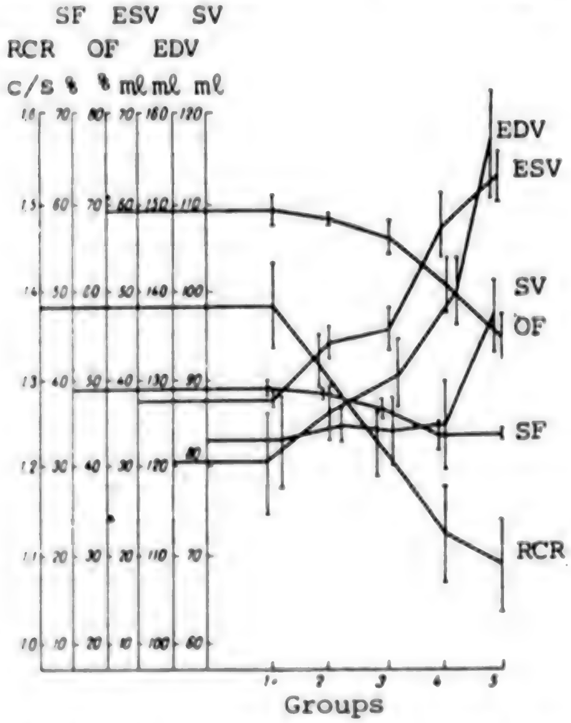
Methods

We examined 58 essentially healthy individuals 22-82 years of age, who presented no complaints referable to the cardiovascular system or any serious disturbances that would be demonstrable by conventional clinical methods. The subjects were divided into 5 age groups: the 1st group consisted of 7 people 20-29 years of age (mean age 24.6±0.77),the 2d of 19 people 30-49 years old (38.1+0.90), the 3d of 13 people 50-59 years old (53.2±0.67), the 4th of 8 people 60-69 years of age (63.8±0.79) and the 5th of 11 subjects over 70 years old (74.7±0.90).

We used the conventional method [11, 12] for examining the subjects using an Echoview-80 (United States) echocardiograph. We used an average-focus sensor at a frequency of 2.25 MHz. The sensor was placed in the 4th-6th intercostal space, depending on the subject's body schema and along the parasternal line to the left of the sternum. Concurrently with the echocardiogram, we recorded the EKG in one of the Neba leads. On the echocardiogram, we measured the left ventricular cavity at the end of the systole (Ds) and diastole (Dd) (in cm), systolic and diastolic excursion of the posterior wall of the left ventricle and interventricular septum, as well as time of contraction and relaxation of these structures. We then calculated the end systolic (ESV) and end diastolic (EDV) volumes of the left ventricular cavity (in milliliters) by the formula of Teichholz et al. [13], stroke volume of the heart (SV) (in milliliters), output fraction (OF) and fraction of reduction of anteroposterior size (%) of the left ventricle (SF), rate of circular [?]reduction of myocardial fibers (RCR) (in circumferences per second), as well as mean rate of contraction (CRpw, CRs) and relaxation (RRpw, RRs) of posterior wall of the left ventricle and interventricular septum.

Results and Discussion

The results of our study are listed in the Table. On the whole, our data conform with those known in literature sources [8, 10-12, 14, 15].



Age-related dynamics of the main echocardiographic parameters (key: c/s--circumferences/second)

We demonstrated age-related differences in echocardiographic parameters. Thus, as compared to those of the 1st group of individuals, in the 3d-5th groups the size of the left ventricular chamber in systole and diastole was reliably ($P<0.05$) increased. There was more marked increase in ESV than EDV: ESV in the 3d, 4th and 5th groups was greater by 23.1, 47.6 and 59.8% ($P<0.05$) than in the 1st group and EDV was 8.2, 16.3 and 30.0% greater, respectively. SV increased insignificantly; however, it was 16.5% greater in the 5th group ($P<0.05$) than in the 1st group of subjects. With age there was a decrease in parameters characterizing contractility of the myocardium. Thus, while OF and SF were only 1.6 and 2.1% lower in the 2d group than the 1st, these parameters decreased by 18.7 and 12.2% in the 5th group. There was more appreciable decline of RCR of myocardial fibers, i.e., the parameter that directly reflects contractility of the myocardium. As compared to the parameters for the 1st group, subjects in the 3d, 4th and 5th groups presented 10.9, 18.1 and 21.0% decreases, respectively, in RCR ($P<0.05$).

As can be seen in the Figure, distinctive "scissors" are formed between the volumetric parameters of the left ventricular chamber and myocardial contractility, i.e., the volume parameters increase with age while contractility of the myocardium decreases.

Analysis of the rate of displacement of the walls of the left ventricle revealed that there was a reliable ($P<0.05$) decrease in mean RRpw with age. But CRpw and CRs showed virtually no change. We even observed some increase of CRs and RRs.

Thus, the decline with age of echocardiographic parameters, myocardial contractility and increase in size and volume of the left ventricular chambers are indicative of the fact that the functional capabilities of the cardiovascular system diminish, even in essentially healthy people.

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ROLE OF POLARIZATION AND RESONANCE IN ASSESSING THE BIOLOGICAL EFFECTS OF ELECTROMAGNETIC RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 18 Jun 81) pp 84-87

[Article by A. A. Galkin]

[English abstract from source] The dosimetric concept of measurements of electromagnetic radiations (EMR) during irradiation of biological objects can be realized by methods of mathematical modeling of EMR interactions with biological objects, which can be represented as an image of the human body as a uniform ellipsoid of revolution. The efficient surface of EMR absorption for the models shows a marked resonance dependence on the radiation frequency. The ratio of the largest to the smallest axes of the ellipsoid of revolution can be used as a resonance criterion. Besides, radiation polarization needs to be taken into consideration. This paper discusses the frequency dependence of the efficient absorption surface for three major types of radiation polarization. The paper demonstrates an applicability of the calculation method to the evaluation of the EMR absorbed dose rate.

[Text] In recent years, a stricter approach has been adopted to quantitative estimation of the physical parameter of interaction in studies of the biological effects of electromagnetic radiation (EMR).

In addition to radiation power density, the parameter of absorbed dose rate (in W/kg) and radiation dose (J/kg) have begun to be used frequently in the literature [1, 2]. These parameters make it possible to work with concrete dosimetric concepts in radiobiology referable to the nonionizing radiation spectrum. One must overcome some difficulties, which are related to the distinctions of absorption of electromagnetic energy (EME) in living tissues of man and animals.

Most biological materials are weak magnets. This determines the predominant role of electric properties of tissular material and advances to the fore evaluation of the electric component of EMR when it interacts with a biological object.

We know from general EMR theory that the link between electric and magnetic intensities can be determined by means of Maxwell's equations, which contain the concepts of charges and currents. One of the derivations of the second equation is the thesis that the tangent component of the intensity vector of an electric field on the interface between two media is continuous [3]. Maxwell's equation, like the basic conceptions of mathematical radiation field theory, can serve as the basis for development of dosimetry in electromagnetic fields (EMF).

Several theoretical and experimental studies were pursued to solve the problem of dosimetry [4-6]. However, they did not cover all of the questions. In particular, insufficient analysis was made of the causes of appearance of so-called resonance absorption of EME [electromagnetic energy] by biological objects or explanation of polarization effects. The relation of resonance frequency to the main dimensions of man has not been sufficiently demonstrated; the role of effective absorption surface (EAS) has not been specifically defined as it relates to changes in radiation frequency. For this reason, some of the recommendations referable to estimation of absorbed energy [6, 7] may appear insufficiently validated.

One can obtain sufficient accuracy in estimating dosimetric parameters for human models, using the concept of a homogeneous ellipsoid of rotation [7]. Figure 1 illustrates such a model, where the large and small axes of the cross-section ellipse along the large axis constitute $2a = L$ and $2b$, respectively. According to conventional conceptions, the total surface of an ellipsoid equals [8]:

$$A = 2\pi\left(b^2 + \frac{ab}{\varepsilon}\arcsin\varepsilon\right), \qquad (1)$$

where $\varepsilon = \sqrt{1 - \frac{b^2}{a}}$. The area of cross-section along the main axis [8] is:

$$A_{\text{shadow}} = \pi ab. \qquad (2)$$

The length of the ellipse curve is $1.1\pi(a + b)$ [9]. The mass of an ellipsoid with density ρ equals

$$G = {}^4/_3\pi ab^2\rho. \qquad (3)$$

The dose absorbed by the ellipsoid model can be expressed as follows:

$$M = S_{\text{eff}}I/G, \text{ W/kg}$$

where S_{eff} is EAS, m^2, I is EMR intensity, W/m^2 and G is the ellipsoid mass, kg.

As we see, the main difficulty in practical application of the last equation is referable to calculation of EAS. This parameter is affected by the resonance conditions of EMR absorption, polarization and total surface of the model (ellipsoid).

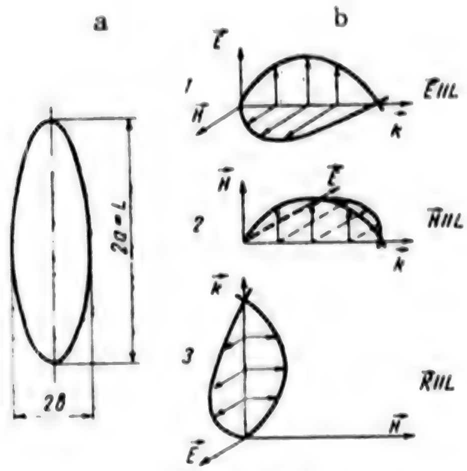

Figure 1.
Model of biological object (a) and types of polarization (b)
1) longitudinal
2) longitudinal-transverse
3) transverse

It is known [1] that the characteristic parameter for certain radiation wavelengths and type of antenna is the EAS of the antenna and, conversely, for a selected type of antenna (for example ellipsoid model of animal) the effectiveness of absorption changes drastically with change in radiation frequency. These changes are the most marked in the region of resonance absorption of EME, where the efficiency of a given antenna is at a maximum. For this reason, if we were to consider a fixed antenna (for example, the body of an animal), we would observe its greatest efficiency with change in radiation frequency within a specific frequency range. Moreover, it can be assumed that maximum absorption effectiveness corresponds to EAS that equals the total surface of the model (ellipsoid). This can be achieved only with a specific radiation frequency, which is related to the dimensions of the model.

Let us use as a primary [or first order] criterion to find resonance frequency the Mie scattering theory described in [7, 10], according to which the time of appearance of resonance corresponds to equality of EMR half-wave in free space and the shortest envelope from the center of the anterior half-ellipsoid to the center of the shaded part of its surface.

Qualitative examination of conditions of EMR absorption by the model shows that different degrees of absorption are possible, depending on the orientation of the vector of the electric component of the EMF in relation to the main axis of the ellipsoid. In the case of parallel orientation thereof, there is the largest relative share of tangents to the ellipsoid surface making up the electric vector and this, as we know, permits penetration of electric energy through the interface between air and the biological object without any changes whatsoever. Other types of polarization would have intermediate quantitative values for absorbed electric energy.

Let us consider three types of polarization which take more detailed consideration of EMR absorption at resonance and higher frequencies. Figure 1 illustrates the longitudinal, longitudinal-transverse and transverse polarizations, which reflect the reciprocal position in space of EMR vectors and the main axis of the ellipsoid. As we mentioned above, longitudinal polarization differs qualitatively from the others, which has also been confirmed experimentally [11]. The other two types of polarization do not present any particular differences from one another and, in the first approximation, can be considered the same from the standpoint of numerical value of resonance frequency. However, as shown by measurements [12], relative absorption at the resonance frequency is twice as great for transverse polarization as for longitudinal-transverse.

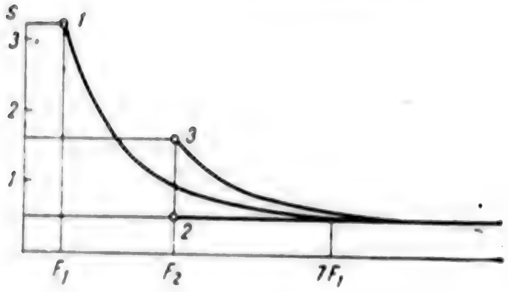

Figure 2.
Relative EMR absorption (S) for an elliptic model
F_1) resonance frequency with longitudinal (1) polarization
F_2) the same with longitudinal-transverse (2) and transverse (3) polarization
$7F_1$) value on x-axis, with which there is disruption of relative absorption (S) as a hyperbolic function of EMR frequency

One can find the numerical value of resonance absorption frequency for different types of polarization from the corresponding values of length of elliptic curve and circumference determining the shortest route for waves enveloping the biological object.

Thus, with longitudinal polarization, resonance is a function of b/λ:

$$L/\lambda = 0.29/(1 + 2b/\lambda). \qquad (5)$$

For a man of standard height (170 cm) and weight (70 kg) [13], $L/\lambda = 0.23$. At the same time, for other types of polarization that are unrelated to the ratio of small to large axes of the ellipsoid the resonance wavelength is defined as:

$$L/\lambda = 2/\pi = 0.64. \qquad (6)$$

Some theoretical and experimental works [5, 7, 12, 14] have shown that one can expect for EAS only one resonance EME absorption, a criterion for which is the L/λ ratio, in the entire spectrum of EMR in the superhigh frequency range (SHF). The maximum value of EAS varies for different types of polarization. In the case of longitudinal polarization it is close to the complete surface of the ellipsoid; for longitudinal-transverse polarization it is virtually constant over the entire SHF range and, as we have already mentioned above, for transverse polarization at the resonance frequency the relative absorption is twice the asymptotic value of other, higher frequencies. There has been experimental confirmation of these conclusions, both when measured on phantoms and in animal experiments [5, 11, 12].

The area of the ellipsoid shadow of 0.5 serves as a warranted EAS asymptote at a sufficient distance from resonance absorption. An analogous pattern was noted in early theoretical studies with spherical models [15, 16]. With a change in frequency from the resonance level to 7 times higher, the EAS changes in accordance with the hyperbolic law. This was also experimentally confirmed by Gandhi et al. [12].

Determination was made of resonance EMR frequencies for a model of a "standard" average man 170 cm tall weighing 70 kg (the large and small axes of the ellipsoid of revolution constituted 85 and 21 cm, respectively, $A = 0.561\ m^2$, $A_{shadow} = 1.8\ m^2$, $L/2b = 4.05$): 41 MHz for longitudinal polarization and 114 MHz for the other two types of polarization.

Figure 2 illustrates the changes in EAS, in relative units, as a function of frequency:

$$S = S_{eff}/A_{shadow} \qquad (7)$$

when demonstrates the comparative characteristic of EMR absorption in the SHF range.

Thus, the ellipsoid model enables us to reduce estimation of the complicated situation of interaction between EMR and the human body to three main types of polarization, and to calculate absorbed radiation doses with due consideration of the relative coefficient of absorption in the form of parameter S which, in turn, reflects the resonance properties of EMR absorption by biological objects. These views may be useful in the practice of aviation and space medicine, the specifics of which are referable to the considerable nonuniformity of irradiation and relatively high intensity of EMR.

The above discussion is referable to irradiation in free space, without considering reflections from earth, which requires additional determination.

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BRIEF REPORTS

UDC: 629.78:[612.452+612.89

SYMPATHOADRENAL SYSTEM OF COSMONAUTS FOLLOWING 7-DAY FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 12 May 81) pp 88-91

[Article by N. A. Davydova and R. A. Tigranyan]

[Text] The sympathoadrenal system (SAS) is an important element of neurohumoral regulation, and for this reason it is particularly important to study the activity of its hormonal and mediatory elements, which is an indicator of stress reactions, during space flights when the human body is exposed to extreme factors, and the success of the flight depends largely on man's capacity to adjust to these conditions. A number of researchers have examined SAS activity in cosmonauts following flights of various duration [1-4]; however, the results do not reflect adequately the changes occurring in the SAS due to the fact that only some aspects of catecholamine (CA) metabolism were studied. Our objective here was to determine whether a stress reaction could occur following 7-day space flights by using the complete spectrum of parameters characterizing SAS activity.

Methods

We examined the SAS of cosmonauts who had made 7-day flights aboard the Soyuz-36, Soyuz-37 and Soyuz-38 spacecraft.

Soyuz-36: Venous blood was analyzed 35 days before the flight and on the first postflight day; 24-h urine samples were analyzed 34, 3, 2 and 1 day before lift-off, for the first 6 postflight days in the commander (CDR), on the day of landing (0 day) and first 5 postflight days in the scientist-cosmonaut (SPT).

Soyuz-37: Venous blood was examined 30 days before the flight and 1st day after termination thereof; 24-h urine samples were analyzed 30, 29, 28, 3, 2 and 1 day before lift-off, on the day of landing and first 2 postflight days in the CDR, and in the SPT 30 and 3 days before the flight and the first 3 postflight days.

Soyuz-38: Venous blood was examined 30 and 15 days before the flight, on the 1st and 7th days after termination thereof; 24-h urine samples were analyzed 30, 29, 28, 3, 2, 1 day before lift-off and on the first 3 postflight days in the CDR, and 30, 29, 28, 15, 14, 3, 2, 1 day before the flight, 0-day and first 2 postflight days in the SPT.

Epinephrine (E), norepinephrine (NE) of blood, E, NE, dopamine (DA), dopa, metanephrine (MN), normetanephrine (NMN) in urine were assayed by fluorimetric techniques [5-7], while vanillylmandelic (VMA) and homovanillic (HVA) acids in urine were assayed by thin-layer chromatography [8]. Relative activity of different elements of CA metabolism were calculated for qualitative evaluation of SAS state [9].

Results and Discussion

Preflight examination revealed that SAS activity was within the physiological range in all cosmonauts (Figures 1-4).

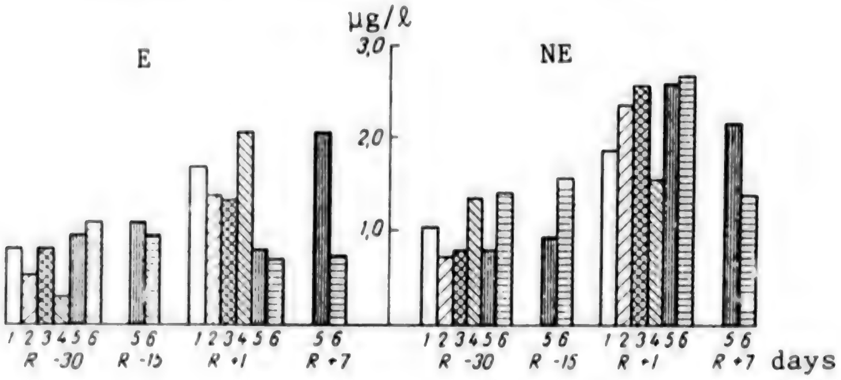

Figure 1. Blood CA content in preflight and postflight periods

1, 2) CDR and SPT of Soyuz-36 spacecraft, respectively
3, 4) the same for Soyuz-37
5, 6) the same for Soyuz-38

Just prior to lift-off, the changes in SAS activity did not deviate significantly from physiological fluctuations; however, all cosmonauts developed an emotional reaction, manifested by activation of the hormonal element of the SAS. This was confirmed by increase in blood and urine E content, decrease in processes of methylation thereof (MN/E) and binding with acid radicals. The E/NE ratio (according to results of urinalysis) had a tendency toward rising, and this was particularly marked in the crew of Soyuz-38 and Soyuz-36 (see Figures 2 and 4).

This systemic reaction was probably related to preparations for space flights, and it had already been reported by a number of researchers with reference to other cosmonauts [3, 10].

After termination of the flights, blood E and NE (see Figure 1), urine E, NE and MN content increased in all cosmonauts, as compared to preflight levels; The percentage of E and NE binding was lower, while that of MN and NMN was higher than before the flights. For example, E excretion rose immediately after landing in the Soyuz-37 crew: to 32.0 μg/day for the CDR and 30.0 μg/day for the SPT, as compared to base values (11.2 and 17.9 μg/day, respectively). VMA and HVA excretion was elevated only in the crew of Soyuz-36, and in the others it remained on preflight levels. E/NE ratio (according to results of urinalysis) was elevated in all CDR's for the first 2 days, followed by a tendency toward decline; in the SPT, elevation of this parameter was brief, more often on 0 or R+1 day, or else there was none at all, as in the SPT of Soyuz-37 (see Figure 3). The process of methylation of E (MN/E) was diminished in all cosmonauts during the entire postflight period (see Figures 2-4). The increase in hormonal activity was probably related to the positive emotions of the cosmonauts upon completion of the flights. The presence of more marked changes in the CDR's was apparently attributable to the fact that they bore greater responsibility for the space missions and successful completion thereof.

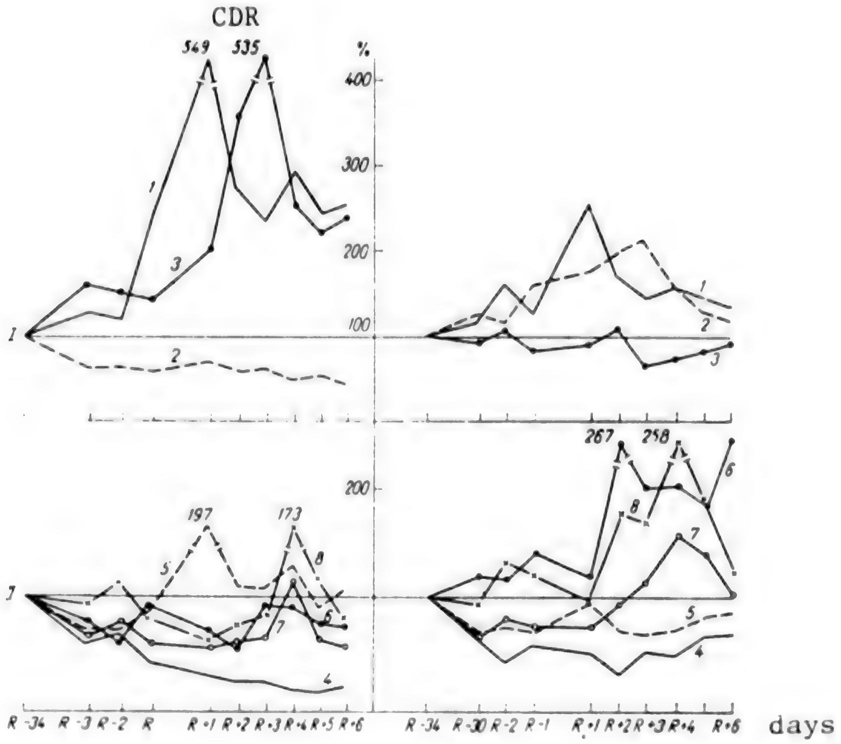

Figure 2. Relative activity of CA and CA metabolite metabolism in the crew of Soyuz-36, preflight and postflight periods

1) E/NE
2) NE/DA
3) DA/dopa
4) MN/E
5) NMN/NE
6) HVA/DA
7) VMA/E + NE
8) VMA/MN + NMN

The results obtained right after the flights (0-1st days) indicate that 7-day space flights do not elicit a marked stress reaction in the cosmonauts. This conclusion was made on the basis of conventional criteria for evaluation of changes in integral parameters of CA metabolism under stress, when there is an increase in general secretory activity of the SAS, level of excretion of free CA in urine, adequate increase in synthesis thereof and relative hypometabolism with adequate conjugation. In our studies, there was an increase in excretion of CA and inactivation thereof; however, this was not associated with changes in the main criterion--activation of CA synthesis. Previously obtained data from studies of cosmonauts who had made short-term flights aboard Soyuz spacecraft also revealed that these missions did not elicit stress reactions [2-4, 10].

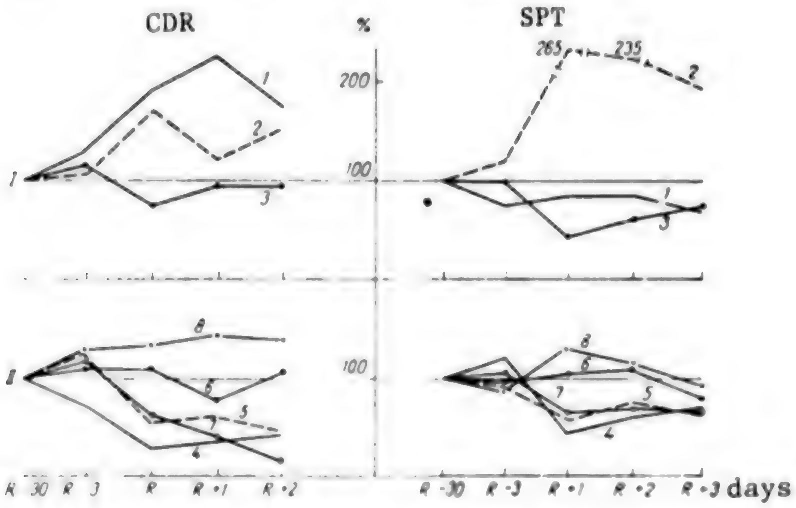

Figure 3. Relative activity of metabolism of CA and their metabolites in the crew of Soyuz-37 in preflight and postflight periods. Parameter levels found 30 days before the flight were taken as 100%.

Changes in activity of the mediator element of the SAS occurred in the following manner. All cosmonauts presented elevation of blood and urine NE; excretion of DA and dopa showed virtually no change, whereas excretion of NMN presented a tendency toward decline. There was a decline of NE/DA ratio in the CDR's of Soyuz-36 and Soyuz-38 (see Figures 2 and 4), whereas in the SPT of Soyuz-38 it did not differ from the preflight level (see Figure 3). Relative activity of NE synthesis (NE/DA) was increased in the crew of Soyuz-37, whereas DA/dopa ratio was diminished (see Figure 3). The DA/dopa ratio was elevated in the crew of Soyuz-38, as compared to prefight levels (see Figure 4). Processes of inactivation of NE (NMN/NE) and DA (HVA/DA) presented a tendency toward decline in the postflight period in all of the cosmonauts (see Figures 2-4). Parameters characterizing overall processes of CA inactivation (VMA/E + NE and VMA/MN + NMN) were above preflight levels (see Figures 2-4), which was probably indicative of a general tendency toward hypermetabolic processes in the postflight period. Thus, there was an increase in activity of the mediator element of the system after completion of the flights in all cosmonauts, but it was not very marked.

The above-mentioned differences in changes in the mediator element of the SAS of cosmonauts are apparently related to individual distinctions of this system, as well as differences in degree of conditioning for space flight factors.

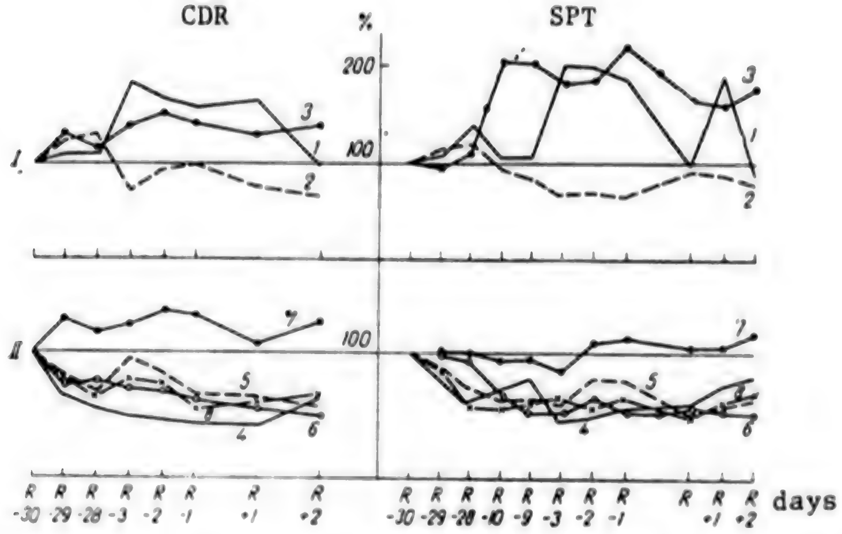

Figure 4. Relative activity of metabolism of CA and their metabolites in the crew of Soyuz-38 in preflight and postflight periods

1) E/NE	3) 3) DA/dopa	5) NMN/NA	7) VMA/MN + NMN
2) NE/DA	4) MN/E	6) HVA/DA	8) VMA/E + NE

Activation of the mediatory element of the SAS had been found previously in cosmonauts who participated in space flights differing in duration, and authors related these changes to the return to earth's gravity after being in weightlessness [1, 2, 4, 10].

It should be noted that we observed rapid normalization of SAS parameters in all of the cosmonauts, which was indicative of rather rapid development of adaptation, and this was related to the good training of cosmonauts for the flights.

Thus, it can be concluded that the results of our study of changes in SAS activity of cosmonauts who participated in 7-day space flights aboard Soyuz spacecraft are indicative of absence of marked stress reactions.

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UDC: 612.116:612.144

VENOUS PRESSURE AS AN INDICATOR OF CIRCULATING BLOOD VOLUME

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 29 Oct 80) pp 91-92

[Article by A. S. Nekhayev, V. A. Degtyarev and V. S. Bednenko]

[Text] The reduction in circulating blood volume (CBV) due to fluid loss in weightlessness can be viewed as one of the defense mechanisms that prevents development of hypertension and hypervolemia in the intrathoracic and cranial parts of the circulatory system. However, upon returning to earth's gravity, this change in CBV could be the cause of decline in orthostatic stability of cosmonauts. For this reason, it is necessary to monitor CBV dynamics in the postflight period, particularly with correction of fluid-electrolyte balance.

Since the existing methods of measuring CBV are complicated, it is interesting to explore the possibility of indirect evaluation of CBV, in particular, by means of the indicator of venous pressure (VP) in the system of jugular veins measured indirectly [1]. This was the purpose of our study.

Methods

A total of 26 healthy male subjects, 19-27 years of age, participated in these studies. VP was determined by a noninvasive method, according to magnitude of vertical projection of the hydrostatic column of blood between the right atrium and sagittal sinus of the skull during passive movement of the subject from horizontal to vertical position at the moment of complete leveling of the presystolic wave on the arteriovenous pulsogram of cervical vessels [1]. Brief increase in CBV was obtained by a well-known method [2, 3] involving rapid intake of water in amounts of 750 and 1500 mℓ, which constituted on the average a volume corresponding to about 1 and 2%, respectively, of body weight. VP was determined before the water load and in the 30th min after fluid intake (at the height of the load). In 11 cases, right after taking VP at the peak load, we assayed initially eliminated urine (IEU). The results of these studies are listed in the Table. We obtained a decrease in CBV by placing inflatable cuffs about the upper third of both thighs [4, 5]. For these tests, we selected a group of subjects with higher base VP (close to levels observed in cosmonauts in weightlessness [6]) in order to test the efficacy of such a factor on venous hemodynamics. The pressure in the cuffs was raised until pulse disappeared over peripheral arteries of the feet and legs, then lowered somewhat until the first distinct pulsations appeared, and kept on this level for 5 min. We monitored the compression by means of a mercury pressure gauge connected into the pneumatic system of the cuffs. It usually constituted 80-100 mm Hg and provided for integrity of arterial influx with impairment of efflux of blood through the superficial and deep veins. VP was taken before applying the cuffs and in the 5th min after creating compression.

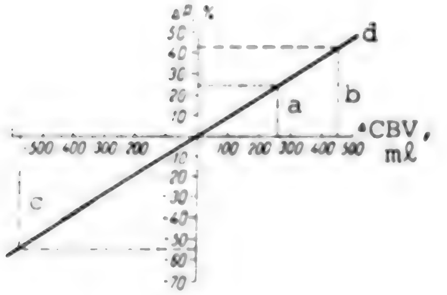
Results and Discussion

Our results are listed in the Table. Analysis of primary data shows that no VP dynamics were observed with a 1% water load in 53% of the cases, and this was apparently related to the initial fluid balance or distinction of distribution of excess fluid in the fluid sectors and rapid elimination thereof. This is indicated, in particular, by the higher IEU, the mean level of which was 25% higher with the 1% water load than the 2% test. In the other cases, VP rose but by no more than 25%.

Changes in VP and amount of IEU related to the functional tests

Test	Number of subjects	Number of cases	VP, mm Hg		P	IEU, mℓ
			initial	during test		
Water load, 1%	9	19	4,8±0,5	6,0±0,6	>0,05	119±13
Water load, 2%	9	22	5,5±0,7	8,1±0,8	<0,05	95±8
Compression of lower limb veins	17	17	9,6±0,9	4,3±0,6	<0,06	—

Note: Mean VP in 30th min of test is given.



CVP (ΔP, %) as a function of CBV (ΔCBV, mℓ)

a, b) changes in parameters with 1 and 2% water loads, respectively

c) compression of veins of lower extremities

d) according to data in [9]

VP rose in 82% of the cases with a 2% load. The mean increment constituted 47%. These data indicate that the dynamics of VP measured in the jugular vein by an indirect method reflects well the increase in CBV. The results obtained with the 2% water loads are more graphic.

Measurement of VP in the case of diminished CBV, caused by application of compression cuffs on the lower limbs, showed a drop in pressure of all subjects (by a mean of 55%). Thus, elimination of blood deposited in the lower extremities from actively circulating blood causes a significant drop of VP in the jugular veins, which confirms the efficacy of using compression cuffs for brief prevention of redistribution of blood in a cranial direction in cosmonauts, as well as the feasibility of using the VP for qualitative evaluation of CBV deficiency. Since it has been reported by A. A. Adenskiy [7] that pressure drops rapidly and to a greater extent in the inferior vena cava and both jugular veins with decrease in CBV, it can be assumed that monitoring VP in the jugular veins would permit detection of early CBV changes. Our results are very consistent with data that confirm the link between central venous pressure (CVP) and CBV level [8, 9]. A. N. Berkutov [8] demonstrated a proportionality between CVP and CBV, which was impaired only when CVP was less than 1 cm water column (about 0.7 mm Hg). Similar findings were made by Echt [9], who studied the dynamics of CVP in healthy subjects with ±500 mℓ change in CBV (see Figure). After intravenous infusion of 500 mℓ blood substitute, CVP increased by almost 1.5 times, whereas with infusion of the same amount of blood it decreased to one-half. Using our data on VP changes and the function described by Echt, one can estimate that CBV briefly increases by 250 mℓ with intake of 750 mℓ water and by 450 mℓ with intake of 1500 mℓ. Compression of the veins of the lower extremities is associated with about 500-mℓ decrease in CBV.

As shown by the results of previous studies [1], the method of taking VP used here is accurate to ±16%, as compared to direct manometry of pressure in the jugular vein. It can be considered quite satisfactory for taking VP under dynamic conditions, in particularly with the above-mentioned changes in CVB, since the range of changes in pressure in the jugular veins with the use of water load tests and compression of veins of the lower limbs is considerably wider than the range of measurement errors.

Thus, on the basis of our findings, it can be concluded that VP can be used for fine evaluation of CBV dynamics.

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ELECTROMETRIC CHARACTERISTICS OF MAN'S GASTROLINGUAL REFLEX

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 (manuscript received 1 Jun 81) pp 92-93

[Article by I. Ya. Yakovleva]

[Text] Soviet and foreign physiologists have demonstrated that the interoceptive system of the stomach activates gustatory receptors [1-3].

There are only isolated works dealing with the distinctions of regulation of activity of man's gustatory receptors [4, 5]. The authors studied the gastrolingual reflex (GLR) using solutions of flavored substances (sweet, salt, acid and bitter). However, because of the difficulty and laboriousness of such studies, analogous methods did not gain use in clinical practice. At the same time, electrogustometry, which permits rapid quantitative determination of taste reception [6, 7], could also be used to evaluate gastrolingual interaction.

Our objective here was to use electrometry of the taste analyzer to characterize man's GLR in the presence of usual gravity and with alteration of earth's gravity.

Methods

GLR was measured in microamperes, from the difference between threshold sensibility of taste receptors of the tongue to electrostimulation after intake of food and fasting. Threshold sensitivity of gustatory receptors to gradually increasing direct current was tested on the tip of the tongue, 1.5 cm to the right of the midline, on a fasting stomach and 10-15 min after a meal. We tested healthy men 25-45 years of age. A total of 53 men were tested (in seated position) at the usual level of earth's gravity and 9 men were additionally kept for 3 h in antiorthostatic position (head end of bed tilted to -8° angle). They took meals without disruption of antiorthostatic body position.

Results and Discussion

According to the obtained data, the electrogustometry parameters determined on a fasting stomach with the body erect (sitting down) ranged from 13 to 65 μA constituting a mean of 32.9±2.64 μA. After intake of food, the taste threshold rose in all subjects to 22-69 μA, the mean being 39.1±3.03 μA ($P<0.01$), or 118.8% compared to fasting gustatory threshold taken as 100%. According to data in the literature, the rise of gustatory threshold after intake of food is characterized as a positive GLR [4, 5, 7]. Quantitatively, the GLR was determined from the difference between postprandial and fasting taste thresholds. In seated position, GLR ranged from 4 to 9 μA, constituting a mean of 6.1±2.7 μA. After 3 h of exposure to an altered gravity field, which was created by remaining in bed with the head tilted down, preprandial taste threshold constituted a mean of 69.3±0.8 μA ($P<0.01$) and considered as 100% for altered gravity field. Intake of food in antiorthostatic position did not alter sensitivity of gustatory receptors of the tongue to electrostimulation in two subjects. Postprandial gustatory threshold dropped by 9-12 μA in antiorthostatic position and constituted a mean of 58.1±1.5 μA ($P<0.01$), or 83.8% of the base level recorded in antiorthostatic position. The GLR changed accordingly, became negative and ranged from -5 to -14 μA, the mean being -11.2 μA.

Thus, 3 hours of antiorthostatic position was associated with a change in GLR in all 9 subjects: depression of this reflex in 2 cases and change in its direction in 7. Intake of food was associated with a decline, rather than rise of gustatory threshold. Analogous changes in GLR under conditions of antiorthostatic hypokinesia (AOH) had been noted in studies of taste using flavored solutions [5]. These functional changes in the gustatory analyzer and in its interaction with the stomach could be attributable to a number of the physiological effects associated with antiorthostatic position.

The redistribution of blood and body fluids to the upper half of the body, which is specific for these conditions, was associated with venous plethora of the head and change in microcirculation, both in the region of the receptor system and central parts of the taste analyzer. Both these factors could apparently affect the function of the gustatory organ. At the same time, we cannot rule out the influence of altered analyzer interaction under AOH conditions, since a gustatory sensation is formed through interaction of taste organs, olfactory organs, tactile receptors and under the regulatory control of the central nervous system. Changes have been repeatedly demonstrated in tactile reception and the central nervous system under AOH conditions [8].

Thus, our results revealed that exposure of healthy man to conditions simulating the period of acute adaptation to weightlessness is associated with impaired function of the taste organ and is characterized by a change in the GLR.

Electrometric studies of taste can be used for determination of quantitative characteristics of gastrolingual interaction.

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CURRENT EVENTS AND INFORMATION

NINTH WORLD CONGRESS OF CARDIOLOGISTS SCHEDULED

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 pp 94-95

[Article by editorial board]

[Text] The 9th World Congress of Cardiologists will convene in Moscow on 20-26 June 1982.

We are very pleased to invite you, on behalf of Soviet scientists and physicians, to participate in the work of the 9th World Congress of Cardiologists.

At present, there is an epidemic of cardiovascular disease in the world, which takes millions of lives on all of this planet's continents. It ignores borders, age and nationality differences. In order to overcome it, we must all join forces. The International Society of Cardiologists was founded for this purpose. Thirty years have passed since the First International Congress of Cardiologists convened in Paris. Much has changed in these years--our views about a number of diseases, our diagnostic and therapeutic capabilities. The International Society of Cardiologists and its congresses, which sum up achievements and are a stimulus for new research, have played a sizable role in this process.

We hope that prominent scientists of the world will gather at the 9th World Congress of Cardiologists in Moscow, and that it will be another phase in the development of modern cardiology.

On behalf of Soviet cardiologists, I should like to thank the International Society and Federation of Cardiologists for granting me the honor of organizing the 9th World Congress in Moscow, and thank all those who will participate in this congress, as well as assure them that the Organizing Committee and Soviet physicians will do everything to organize it better and provide the traditional Russian, sincere welcome.

[from] Academician Ye. Chazov,
President of the 9th World Congress of Cardiologists

The main scientific topics to be covered by the congress are as follows:

Lectures

1. Development of echocardiography.
2. Development of radionuclide examination methods.
3. Cellular and molecular mechanisms of development of atherosclerosis.
4. Could a change in life style prevent development of atherosclerosis?
5. Are there pathophysiological markers of hypertensions?
6. Control and treatment of hypertension.
7. Cardiomypathy: pathology and infectious-immunological mechanisms.
8. Treatment of cardiomyopathy.
9. Significance of systemic and local factors in arterial thrombogenesis: thrombocytes, prostaglandins and hypotheses.
10. Study of antithrombosis agents.
11. Noninvasive methods of assessment in rehabilitation of cardiological patients.
12. Is it expedient to detect and eliminate arrhythmias?
13. Old and new drugs for treatment of arrhythmia.
14. Calcium transport and cardiovascular disease.
15. Energy metabolism of the ischemic heart.
16. Atherosclerosis and high arterial pressure--a pediatric problem.
17. New surgical approaches to congenital heart disease.
18. The heart during space flights.
19. Transluminal angioplasty for arterial disease.

Symposiums

1. Problems of moderate arterial hypertension.
2. Treatment of arterial hypertension.
3. Mechanisms of development of arterial hypertension.
4. Lipoproteins and atherosclerosis.
5. Significance of the vascular wall, thrombocytes and humoral factors in atherogenesis and thrombogenesis.
6. Detection of prethrombotic states.
7. Macrocirculatory and microcirculatory disturbances in the presence of myocardial lesions.
8. Sudden death: precursors and prevention.
9. Correlation between cerebrovascular and heart diseases.
10. Restricting extent of myocardial infarction in patients.
11. Metabolic protection of the myocardium.
12. Prevention of the main cardiovascular diseases: role of WHO.
13. Results of studies dealing with primary prevention of cardiac ischemia.
14. Cardiovascular diseases in developing countries.
15. Rehabilitation of cardiological patients: results of long-term follow-ups and economic aspects.
16. Static (dilated) cardiomyopathy.
17. Infectious endocarditis.
18. Problems of hypertrophic cardiomyopathy.
19. Pulmonary circulation in the presence of congenital heart disease.
20. Rheumatic heart disease in young people.

21. Evaluation of aortocoronary shunts.
22. Valvular surgery.
23. Heart transplants, artificial heart, extracorporeal ["ancillary] circulation.
24. Emergency cardiology.
25. Electrophysiology of arrhythmias.
26. Pacemakers and surgical management of rhythm disorders.
27. Load tests.
28. Echocardiography.
29. Radionuclide ventriculography and perfusion scintigraphy: advantages and flaws.
30. Radionuclide methods for measuring blood flow.
31. New drugs for treatment of static cardiac insufficiency.
32. Repeated evaluation of digitalis.
33. New approaches to the treatment of cardiovascular disease: immobilized enzymes, liposomes, synthetic peptides.
34. Prostaglandins and cardiovascular disease.
35. Tropical medicine.
36. Pulmonary hypertension and cor pulmonale.
37. Cardiology and dissemination of information among the public.
38. Studies on the care of cardiovascular patients.

ABSTRACTS OF ARTICLES FILED WITH THE ALL-UNION SCIENTIFIC RESEARCH INSTITUTE OF MEDICAL AND MEDICOTECHNICAL INFORMATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 2, Mar-Apr 82 p 96

UDC: 612.017.1

METHOD OF DETERMINING THE FORM OF THE DISCRETE AFFINITY SPECTRUM ACCORDING TO BINDING CURVE

[Abstract of article by V. N. Krut'ko]

[Text] An instrument is described which permits mechanical determination of the form of the discrete function of distribution of affinity (affinity spectrum) of antibody populations on the basis of experimental quantity of bound antigen as a function of total level thereof in a mixture with unchanging antibody content.

The instrument has the following theoretical basis.

According to the law of mass action, for each homogeneous subpopulation of antibodies in a mixture, A_c/A as a function of A_c(A_c and A are amounts of bound and free antigen, respectively, in the mixture) is a straight line M^i:

$$A_c/A = a_i K_i - A_{c_i} K_i, \quad i = \overline{1, I}, \tag{1}$$

where A_{c_i} is the amount of antigen bound with antibodies of the ith subpopulation, a_i is total quantity of antibodies in the ith subpopulation. Determination of the position of lines (1) for all subpopulations is tantamount to determination of the type of discrete affinity spectrum of the population under study. If we were to plote A_{c_i}/A as a function of A_{c_i} and A_c/A as a function of A_c on the same graph, the distance to curve P over any path from the beginning of the system of coordinates will equal the sum of distances to lines M^i, $i = 1, I$.

The design of this instrument makes it possible to find many possible positions $m^i_j \in Op_j$, $i = \overline{1, I}$ for an arbitrary point $p_j \in P$, that will fulfill the condition that points m^i_j belong to lines M^i. At the same time, in the presence of several points p_j, $j = \overline{1, I}$ the instrument provides for all points m^i_j, $j = \overline{1, I}$ to be on the same line, which is the sought M^i line.

Let us find the value of I (number of points p_j) that is necessary and sufficient for determination of the sought set of M^i lines at a given value of I. Let us designate the coordinates of the points: $p_j = (X_j, Y_j)$ and $m^i{}_j = (X^i{}_j, y^i{}_j)$. The points of intersection of the lines with x- and y-axes have coordinates $(a_i, 0)$ and $(0, a_i K_i)$, respectively. Having the above-described features, the instrument gives the following system of links between the coordinates of points $m_j{}^i$ and sought characteristics of spectrum a_i, K_i:

$$(a_i - x^i_j)/y^i_j = a_i/a_iK_i),\ I=\overline{1,\ I};\ j=\overline{1,\ J} \qquad (2)$$

(condition that points $m^i{}_j$ belong to lines M^i);

$$x^i_j/y^i_j = X_j/Y\ ,\ i=\overline{1,\ I};\ j=\overline{1,\ I} \qquad (3)$$

(condition that points $m^i{}_j$ belong to paths $0p_j$);

$$\sum_{i=1}^{I} y^i_j = Y_j,\ j=\overline{1,\ J}, \qquad (4)$$

$$\sum_{i=1}^{I} x^i_j = X_j,\ j=\overline{1,\ J} \qquad (5)$$

(condition of equality of distances to curve P of the sum of distances to lines M^i). It is easy to see that conditions (5) are the consequence of conditions (3) and (4). Expressing $x^i{}_j$, $y^i{}_j$ from conditions (2) and (3) as parameters a_i, K_i, X_i, Y_i and substituting these expressions in conditions (4), we shall obtain a system of correlations between the sought values of a_i, K_i and known X_j, Y_i:

$$Y_j = \sum_{i=1}^{I} \frac{K_i a_i Y_j}{Y_j + K_i Y_j},\ j=\overline{1,\ J}, \qquad (6)$$

each of which is a known expression obtained in describing reactions in a heterogeneous mixture by means of a model of multiple mass action. This system of equations has a single solution when condition $J = 2I$ is met (all points p_j are different). Thus, for unequivocal determination of a spectrum consisting of I M^i lines, we need $2I$ points p_j and the same number of bars in the instrument described here that solves the system of equations (6) mechanically.

Illustrations 2; bibliography lists 8 items.

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